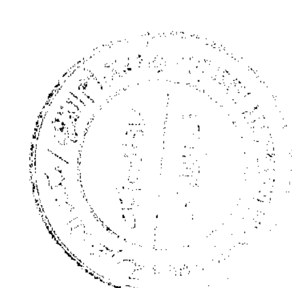
المملكة العربية السعودية
وزارة التعليم العالي
جامعة أم القرى
كلية العلوم التطبيقية
قسم الكيمياء





اصطناع وتطبيق لبعض مشتقات الكينولين الحلقية غير المتجانسة الجديدة

رسالة مقدمه إلى قسم الكيمياء- كلية العلوم التطبيقية
جامعة أم القرى بمكة المكرمة

من

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أستاذ الكيمياء العضوية- قسم الكيمياء
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١٤٢٤هـ/ ٢٠٠٤م



لِكُلٍّ دَرَجَٰتٌ مِّمَّا عَمِلُوا۟ وَمَا رَبُّكَ بِغَٰفِلٍ عَمَّا يَعْمَلُونَ .

الأنعام: ١٣٢

Kingdom Of Saudi Arabia
Ministry Of Higher Education
Umm AL-Qura University
Faculty Of Applide Science
Chemistry Department

SYNTHESIS AND APPLICATION OF SOME NEW HETEROCYCLIC QUINOLINE DERIVATIVES

Thesis

Presented to the Chemistry Department, Faculty of Applied Science,
Umm-Al-Qura University, Makkah, Saudi Arabia

For the Degree of Doctor of philosophy of Science,
Ph.D. (Organic Chemistry)

Presented by

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NOTE

The candidate Mrs. Nariman M.A. Nahas has attended prerequisite courses for one academic year (1421 AH.), in partial fulfillment for the doctor degree of philosophy of Science (Organic Chemistry), covering the following topics :

<u>First Semester (1421 AH.): (6 hours/week)</u>

1-	Advanced Analytical Chemistry	100/100
2-	Advanced Organic Chemistry	97/100
3-	Advanced Physical Chemistry	95/100

<u>Second Semester (1421 AH.): (6 hours/week)</u>

1-	Inorganic Chemistry	97/100
2-	Advanced Organic Spectroscopy	93/100
3-	Selected Topics in Organic Chemistry	100/100
	Total	582/600

She has passed the examinations of the above courses with excellent grade (97 %).

Supervisor of the post graduate studies — Head of Chemistry Department

Prof. Dr. Ali A. Abdel Hafez — Prof. Dr. Abdul Hady M. Soman

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Nariman M.A. Nahas

Contents

Summary

SUMMARY

The work presented in this thesis involves the synthesis and reactions of a variety of tri-, tetra- and pentacyclic heterocyclic quinoline derivatives of potential biological interest.

The pyrano[3,2-h]quinoline derivatives **218**$_{a-e}$-**219**$_{a-e}$ were used as starting materials in our synthetic studies and were used as key intermediate in the synthesis of fused heterocyclic systems. Thus the pyrimido[4`,5`:6,5]pyrano[3,2-h]quinolines (**220**$_{a-e}$-**222**$_{a-e}$) were produced when compounds **218**$_{a-e}$ were reacted with acetic anhydride/pyridine mixture, formamide and formamide/formic acid mixture respectively.

4-Aryl-3-cyano-6-chloro-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]quinolines (**223**$_{a-e}$) were obtained by refluxing compounds **218**$_{a-e}$ with triethyl orthoformate; these compounds **223**$_{a-e}$ underwent aminolysis and cyclization by treatment with aniline to give the corresponding derivatives **224**$_{a-e}$. Interaction of **218**$_{a-e}$ with ethyl cyanoacetate led to the formation of pyridopyranoquinolines **225**$_{a-e}$. However, compounds **218**$_{a-e}$ gave the corresponding triazine derivatives **226**$_{a-e}$ by means of diazotization with sodium nitrite in AcOH/HCl mixture.

Imidazopyranoquinolines **227**$_{a-e}$ could be obtained by the reaction of compounds **218**$_{a-e}$ with ethylenediamine. Cyclization of compounds **227**$_{a-e}$ with triethyl orthoformate, aldehydes and ketones gave the corresponding derivatives **228**$_{a-e}$-**230**$_{a-e}$, respectively. While, the reaction with cyclic ketones and carbon disulfide gave the spiro and thioxo derivatives **231**$_{a-e}$-**233**$_{a-e}$ respectively.

Moreover, interaction of compounds **218**$_{a-e}$ with nitrous acid gave the dichloro derivatives **226**$_{a-e}$ which in turn, proved to be a useful intermediate. Compounds **235**$_{a-e}$- **236**$_{a-e}$ were produced from the reaction of **234**$_{a-e}$ with formic acid and carbon disulfide respectively. In addition, treatment of **234**$_{a-e}$ with acetic acid and sodium nitrite solution at rt gave the azido derivatives **237**$_{a-e}$.

On the other hand, the amino function of compounds **219**$_{a-e}$ were easily converted to the corresponding 1-pyrrolyl group via the interaction with 2,5-dimethoxytetrahydrofurane in boiling acetic acid to give the pyrrolyl ester **238**$_{a-e}$ which reacted with hydrazine hydrate to give the pyrrolyl hydrazide **239**$_{a-e}$. The latter compounds **239**$_{a-e}$ were used for the synthesis of the pyrazolyl and acid azide derivatives **240**$_{a-e}$-**241**$_{a-e}$ by reaction with acetylacetone and nitrous acid respectively.

The acid azide is a versatile compound and could be transformed into a variety of derivatives. When compounds **241**$_{a-e}$ were heated in boiling ethanol, the ethylcarbamates **242**$_{a-e}$ were obtained. When they reacted with hydrazine hydrate gave the semicarbazides **243**$_{a-e}$. Heating the acid azide in a high boiling point solvent such as xylene led to Curtius rearrangement with concomitant ring closure of the isocyanate intermediate **241`**$_{a-e}$ giving pyrrolopyrazinopyranoquinolines **244**$_{a-e}$ which could be transformed into the corresponding chloro derivatives **245**$_{a-e}$ when heated with phosphoryl chloride.

The reactivity of the chlorine atom at C-9 of **245**$_{a-e}$ was shown by its easy displacement using various nucleophilic reagents such as hydrazine hydrate to give the hydrazino derivatives **246**$_{a-e}$. Finally, the triazolo derivatives **247**$_{a-e}$ and **248**$_{a-e}$ were produced from the reaction of **246**$_{a-e}$ with acetic acid and carbon disulfide, respectively.

Some of the newly synthesized compounds were selected for testing of their biological activity, such as antibacterial and antifungal activity. The preliminary results are herein reported.

AIM OF WORK

Heterocyclic chemistry represents one of the major sources for supplying drugs, dyes and chemical industries with new materials. Several correlations have been reported between structure and biological activity is expected to increase biological activity or to develop new ones.

Interestingly, the main target of the presented work is to synthesize some new heterocycles containing pyranoquinoline fused with pyrimidine, triazine, imidazole, pyridine, triazolopyrimidine, pyrrole, pyrrolopyrazine and triazolopyrrolotriazine moieties in an endeavor to develop new materials of anticipated strong biological activities.

Introduction

INTRODUCTION

Heterocyclic compounds are encountered in a very large number of groups of organic compounds. They play a vital role in the metabolism of all living cells, which are widely distributed in nature and are essential to life. Mechanistic investigations enhanced the general understanding of these compounds. Heterocyclic compounds have interesting theoretical implications, diversity of synthetic procedures and physiological and industrial significance. Pyrimidine and purine bases of the genetic material DNA, the essential amino acids, proline, histidine ,tryptophan and the oxygen transporting pigment haemoglobin are some of the important biomolecules which incorporate nitrogen heterocyclic systems in their structures. Also, a large number of nitrogen heterocyclic compounds find varied applications as dyestuffs, plant-growth regulators, agrochemicals, herbicides, reductive antibacterial and antitumour agents.

In connection with the search for newer physiologically active compounds, several reports have appeared on the synthesis of fused heterocyclic quinoline derivatives which were found to be useful as: antipsychotics,[1,2] antiasthmatics,[3] antibacterial,[4-7] antihypertensive agents,[8] anticoccidials-1,[9] antiplatelet agent,[10] antimalarials,[11] antiulcer,[12] antidiabetic agents,[13] anti-(tumor, atherosclerosis, psoriasis, diabetes and arthritis activities),[14] fungicides,[15-17] herbicides,[18] lipoxygenase inhibitors,[19] inhibitors of MEK enzymes,[20] immunostimulants[21] and immunosuppressants,[22] inhibitors of methionyl t RNA synthase,[23] dopamine D_4 receptor ligands,[24] gonadotropin releasing hormone antagonists,[25] phosphodiestrase IV (PDE) inhibitors,[26] potassium channel openers,[27] PDGF(platelet derived growth factor) receptor and / or LCK tyrosine kinase inhibitors,[28] epidermal growth factor receptor signal transduction inhibitors,[29]cardiovascular activities,[30] steroid receptor modiators,[31] NK-3 and NK-2 receptor antagonsists,[32] effective in the therapy of irritable bowel syndrome,[33] for treating urinary incontinence[34] and inhibitors of steel corrosion in acid media.[35] On the other hand, pyran derivatives exhibit antimicrobial activities,[36,37] antitumor,[38]antichotesteremics and platelet aggregation inhibitors,[39] growth stimulating effects,[40] as immunomodulators,[41] cyclooxygenase-2-inhibitor,[42] leukotriene B4 (LTB_4) antagonsists,[43] hypotensive effect,[44] central nervous system activity,[45] in treating neurological disorders[46] and hypersensitive ailments[47] and in the prevention and treatment of gastrointestinal diseases.[48] Moreover, fused pyrimidines

were found to possess a wide biological activities as antimicrobial,[49,50] antiparkinsonian,[51] anticancer,[52] antivarial,[53] herbicides,[54] leishmanicidal,[55] insecticidal,[56] kinase inhibitors[57-60] and as potential antimycotic agents.[61] Also, a wide range of biological activities has been attributed to fused imidazole and triazines, for instance imidazoles are used as antihypertensive,[62] antiallergic,[63] antibacterial,[64] protein kinase C inhibitors,[65] antidiabetes,[66] carcinogens,[67] analgesic activity,[68] thrombin receptors,[69] vascular damaging agents,[70] GAB A_a receptor complex modiators,[71] insulin resistant improvement agents,[72] immune response modifiers,[73] H3-histamine receptor antagonists,[74] human growth hormone mimetics[75] and proton pump inhibitors.[76] Triazoles and triazines are used as antipsychotic agents,[77] fungicides,[78] antimicrobial,[79,80] herbicides,[81] blood platelet anti-aggregation [82] and cardiotonic agents.[83]

Based on these findings, it was of interest to introduce these biologically active moieties in one molecule, giving rise to a new series of potential biochemically active compounds. Therefore many references are dealing with the synthesis and applications of fused heterocyclic quinoline derivatives which are enough to be collected in several texts. From this point of view, we will restrict the introduction of this thesis on the recently, closely and highly related references to our interest as thienoquinolines, pyrimidothienoquinolines, pyrazoloquinolines, pyranoquinolines, pyrroloquinolines and triazolopyrimidoquinolines.

Preparation of some selected fused heterocyclic quinolines:

The reaction of formylquinoline thione[84] **(1)** with a slightly excess of chloroacetic acid ester gave the corresponding ester **(2)** which undergoes ring closure with sodium methoxide to thieno[2,3-b]quinoline **(3)** (Scheme 1).

CHO
$ClCH_2COOCH_3$
CHO
SCH_2COOCH_3
N H S
1
2
$ClCH_2COOCH_3$ NaOMe
NaOMe
N S $COOCH_3$
3

Scheme 1

It was found that[85-87] the reaction of the chloroethylquinoline **(4)** with thiourea in refluxing ethanol gave the thieno[2,3-b]quinoline **(5)** in good yield (Scheme 2).

H_2NCSNH_2

4 5

Scheme 2

Neelima et al[88] mentioned that the reaction of 2-chloro-3-cyanoquinoline**(6)** with $HSCH_2COOCH_3$ gave a mixture of methyl[3-cyano-2-quinolinylthio]acetate**(7)** in low yield and methyl-3-aminothieno[2,3-b]quinoline-2-carboxylate **(8)** in a good yield (Scheme 3).

$HSCH_2COOCH_3$ / DMF/K_2CO_3 ; EtOH /pip. / Δ

6 7 8

Scheme 3

Also, compound **(6)** was converted into furothienoquinoline[89] **(9)** by thiation, followed by two cyclocondensation reaction with $ClCH_2CN$ (Scheme 4).

6 Thiation 9

Scheme 4

Raja[90] reported that upon refluxing of vinylquinolinethiones **(10)** with sodium hydroselenide in EtOH gave thieno[2,3-b]quinoline **(11)** (Scheme 5).

NaHSe / EtOH

10 11

Scheme 5

Recently[91], the reaction of 2-chloro-3-formyl-7-methylquinoline **(12b)** with $HSCH_2COOEt$ in EtOH containing anhydrous Na_2CO_3 gave 2-ethoxycarbonyl-7-methylthieno[2,3-b]quinoline **(13)** (Scheme 6).

a) R = H, b) R = CH_3

Scheme 6

The thieno[2,3-c]quinoline[92] **(15)** was prepared by reacting 2-formyl-3-thiopheneboronic acid **(14)** with 2-bromoaniline in the presence of $(Ph_3P)_4Pd$ as a catalyst in basic medium (Scheme 7).

Scheme 7

Sauter et al[93] found that the application of Skraup reaction to 6-aminobenzo[b]-thiophene led to the formation of the thieno[3,2-f]quinoline **(17)**. However, the reaction of **(16)** with ethoxymethylene diethylmalonate gave compound **18**, which was cyclized via Gould-Jacobs reaction to give thieno[3,2-f]quinoline derivative **(19)** (Scheme 8).

Scheme 8

The cyclization[94] of benzothiophenes **(20)** with EtOCH:C(CO_2Et)$_2$ followed by ester hydrolysis gave the thieno[3,2-g]quinoline(**21)** (Scheme 9).

Scheme 9

Sasaki et al[95] reported that the thioquinoline derivative **22** underwent photocyclization via its enolic form to give **23** (Scheme 10).

Scheme 10

Recently[96] it was reported that 3-cyanoquinoline-2(1H)thione **(24)** was reacted with some halo compounds to give S-substituted thioquinoline derivatives **25,29** and **30**. Cyclization of **30** yielded thienoquinoline **31**. Also, reaction of **24** with chloroacetone, chloroacetonitrile, ethyl chloroacetate and chloroacetamide furnished thienoquionlines **26,27,28** and **31** respectively (Scheme 11).

Scheme 11

Moreover, compound **27** and **31** underwent different sequence reaction to give some new pyrimido-and triazino[4',5':4,5]thieno[2,3-b]quinoline derivatives **(32-44)** (Scheme 12-14).

Scheme 12

Scheme 13

Scheme 14

Bakhite[97] mentioned that a series of new 3-cyano-5,6-dihydro-4-(2-furyl)-2-(substituted)thio-benzo[h]quinolines(**45_{a-c}, 46, 47, 49_{a-e}** and **51_{a-e}**) have been prepared from 3-cyano-5,6-dihydro-4-(2-furyl)benzo[h]quinoline-2(1H)thione **(44).** Compounds **47**, **49_{a-e}** and **51_{a-c}** on treatment with appropriate base underwent smooth cyclization into thieno[2,3-b]benzo[h]quinolines (**48**, **50_{a-e}** and **52_{a-c}**), respectively. Hydrolysis of ester **48** gave the corresponding acid **53** which was converted to oxazinone **54** by heating in acetic anhydride. Oxazinone **54** in turn, was recyclized into pyrimidinone derivatives **55-57** upon treatment with ammonium acetate, hydrazine hydrate and aniline, respectively. Compound **52_{a-c}** were reacted with nitrous acid and with orthoformate to produce the fused polycyclic quinoline derivatives **58_{a-c} – 59_{a-c}**.

48, R= Et
53, R= H

44, Y= furyl

45a-c
a) R= H, b) R= CH_3, c) R= Ph
46, R= CH_2CN
47, R= CO_2Et

49a-e

50a-e

49a-e - 50a-e :R= a)CH_3, b) Ph, c) p-ClC_6H_4, d) p-BrC_6H_4, e) 8-hydroxy-4-quinolinyl

51a-c

52a-c

51a-c - 52a-c: R= a) Ph, b) p-$CH_3C_6H_4$, c) p-ClC_6H_4

54-57

54, Z= O; 55, Z= NH; 56, Z= NNH_2; 57, Z= NPh

58a-c

59a-c

58a-c - 59a-c: Ar= a) Ph, b) p-$CH_3C_6H_4$, c) p-ClC_6H_4

El-Kashef et al[98] reported the synthesis of oxazino[4',5':4,5]thieno[2,3-b]quinoline **(66)**, pyrimido[4',5':4,5]thieno[2,3-b]quinolines **(67-70)**, triazino[4',5':4,5]thieno-[2,3-b]quinolines **(71)** and imidazo[4',5':4,5]thieno[2,3-b]quinolines **(75)** (Schemes 15-21).

60 —a→ 61 —b→ 62; 60 —c→ 62

a. $POCl_3$ b. H_2NCSNH_2, NaOH, HCl c. P_2S_5/pyridine

Scheme 15

62 ⇌ → (ClCH$_2$R) 64, 63

a. R= COOEt b. R= $COCH_3$ c. R= CN d. R= COPh e. R= $CONH_2$ f. R= CONHPh g. R= COHN-C_6H_4-OCH_3 h. R= CONH-(2-pyridyl) i. R= CONH-(4-phenylthiazol-2-yl)

64a → 65 → 66; 64a → 68; 66 → 67; 64e → 68; 64e → 67

a. $NaOH/CH_3OH$ b. Ac_2O c. CH_3COONH_4 d. $HCONH_2$ e. $CH(OC_2H_5)_3/Ac_2O$ f. HCOOH

Scheme 16

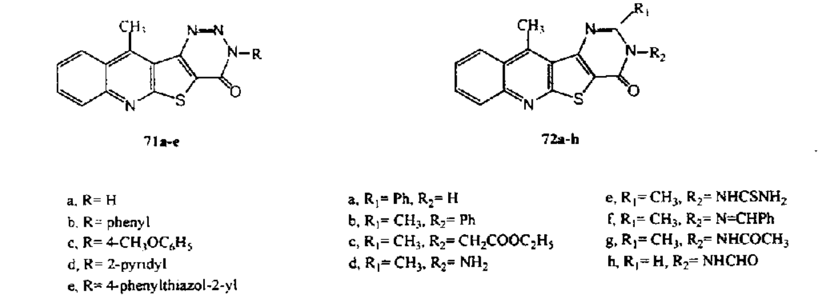
69

a. X= O
b. X= S

70

a. R= H
b. R= phenyl
c. R= 2-pyridyl
d. R= 4-phenylthiazol-2-yl

Scheme 17



71a-e

a. R= H
b. R= phenyl
c. R= 4-$CH_3OC_6H_5$
d. R= 2-pyridyl
e. R= 4-phenylthiazol-2-yl

72a-h

a. R_1= Ph, R_2= H
b. R_1= CH_3, R_2= Ph
c. R_1= CH_3, R_2= $CH_2COOC_2H_5$
d. R_1= CH_3, R_2= NH_2
e. R_1= CH_3, R_2= $NHCSNH_2$
f. R_1= CH_3, R_2= N=CHPh
g. R_1= CH_3, R_2= $NHCOCH_3$
h. R_1= H, R_2= NHCHO

Scheme 18

a, HCOOH, b, $NaNO_2$/AcOH, c, Xylene (reflux), d, $CH_3COCH_2COCH_3$

Scheme 19

a. MeI/AcONa b. $PhCOCH_2Br$ c. MeI, Na_2CO_3/DMF

Scheme 20

a, $CH(OC_2H_5)_3$ b, PhNCO c, $HCONH_2$

Scheme 21

Ring closure of 2-chloro-3-cyanoquinoline **(6)** with hydrazine hydrate proceeded smoothly to yield **83** (Scheme 22).

Ring closure of 2-chloro-3-cyanoquinoline **(6)** with hydrazine hydrate proceeded smoothly to yield **83** (Scheme 22).

Scheme 22

It was reported[99] that on treatment of 2-chloroquinoline-3-carboxaldehyde **(12_a)** with hydrazine hydrate, the pyrazolo[3,4-b]quinoline **(85)** was obtained[99] (Scheme 23).

Scheme 23

The 1H-pyrazolo[3,4-b]quinoline[100] **(85)** was prepared by the reaction of 2-chloroquinoline-3-carboxaldehyde **(12_a)** with hydrazine hydrate by fusion or by heating 2-chloro-3-formylhydrazine **(86)** above its melting point in a sealed tube. Similarly 1-phenylpyrazolo[3,4-b]quinoline **(88)** was obtained by using phenylhydrazine under the same conditions (Scheme 24).

Scheme 24

Also, 1H-pyrazolo[3,4-b]quinoline **(85)** reacted with formaline yielded 1-hydroxymethylpyrazolo[3,4-b]quinoline **(89)**. The Mannich bases **91** were not performed via classical Mannich reaction but were prepared via an indirect pathway involving the formation of compound **89** at first, followed by treatment with thionyl chloride to give the unstable compound 1-chloromethylpyrazolo[3,4-b]quinoline **(90)**. This latter compound **90** was reacted directly with the proper secondary amine to afford the required Mannich bases **91**(Scheme 25).

85 → (HCHO, EtOH) → 89 (CH_2OH) → ($SOCl_2$) → 90 (CH_2Cl) → (sec. amine) → 91 (CH_2R)

91: R=piperidino, morpholino, N-methylpiperazino, dibenzylamino

Scheme 25

Treatment of compound **85** with ethyl bromoacetate, then with hydrazine hydrate gave the pyrazolo[3,4-b]quinoline-1-aceto hydrazide **(92)**. The latter reacted with carbon disulphide and sodium hydroxide in ethanol gave 1-(5-thioxo-4H-1,3,4-oxadiazolo-2-yl)methylpyrazolo[3,4-b]quinoline **(93)**. Alkylation of compound **93** with alkyl or aralkyl halide gave the corresponding alkylthio or aralkylthio derivative **94**, while its reaction with formaline afforded the corresponding N-hydroxymethyl derivative **95**, which was reacted with thionyl chloride followed by secondary amine yielded the Mannich bases 1-(4-substituted aminomethyl-5-thioxo-4H-1,3,4-oxadiazol-2-yl)-methylpyrazolo[3,4-b]quinoline **(96)** (Scheme 26).

Scheme 26

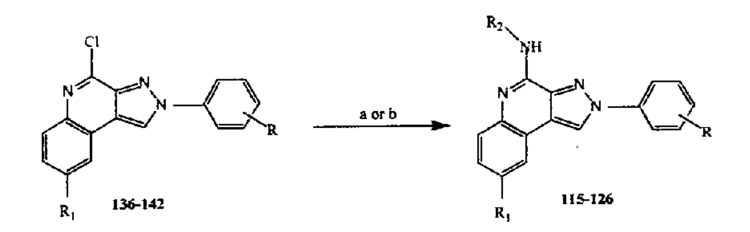
Cupta et al[101] studied the synthesis and structure activity relationships of a new set of 2-arylpyrazolo[3,4-c]quinoline derivatives. The synthetic pathway which yielded compounds **97-133** are illustrated in (Schemes 27-29). The synthesis of **97, 98, 100-103** and **105** which were originally prepared as benzodiazepine receptor ligands has already been reported[101]. The 2-(2-methylphenyl) derivatives **99** and its 2-(4-chlorophenyl) analogue **104** were obtained by reacting the 3-ethoxalyllindole[102] with arylhydrazine hydrochlorides as described to prepare **97, 98** and **100-103**. The 5-N-propyl derivative **106** ensured by the reaction of **97** with n-propyl bromide following the procedure described to prepare **102.**[101] Reaction of **97** and **100-103** with a mixture of $PCl_5/POCl_3$ and pyridine afforded the 1-(2-aryl-2H-pyrazolo[3,4-c]quinoline-4-yl)pyridinum chlorides **(132-135)**, while the reaction of **97-102** and **104** with a neat mixture of $PCl_5/POCl_3$ gave the 2-aryl-4-chloropyrazolo[3,4-c]quinolines **(136-142).** It must be noted that both the pyridinum salts **132-135** and the 4-chloro derivatives **136-142** were unstable; nevertheless they were pure enough to be spectroscopically characterized and used without further purification. Refluxing **132-135** with an excess of cyclohexylamine gave the 2-arylpyrazolo[3,4-c]quinolin-4-amines **(107 and 111-113).** Compound **107** was also obtained with more satisfactory yields from its corresponding 4-chloro derivative **136** and ammonia. Thus, the other 4-amino derivatives **108-110** and **114** were prepared following this pathway, i.e., from the corresponding 4-chloro intermediates **137-139 , 142** and ammonia (Scheme 27).

Allowing the 4-chloro intermediates **136-142** to react with suitable amines gave the 4-N-cycloalkylamines **115-124** , 4-N aralkylamines **125** and **126** (Scheme 28). Finally, Scheme **29** depicts the reaction of 2-phenylpyrazolo[3,4-c]quinolin-4-amine **(107)** with suitable acyl chlorides or phenylacetic acid, or with suitable isocyanates, to afford the 4-amido **127-129** , 4-ureido derivatives **130** and **131**, respectively.

	R	R_1		R	R_1
97,107,136	H	H	**101, 111, 140**	4-Me	H
98, 108, 137	H	Cl	**102, 112, 141**	3-F	H
99, 109, 138	2-Me	H	**103, 113**	4-OMe	H
100, 110, 139	3-Me	H	**104, 114,142**	4-Cl	H

(a) NaH, R_1X, DMF; (b) $PCl_5/POCl_3$, pyridine; (c) $PCl_5/POCl_3$; (d) method A: cyclohexylamine; e) method B: NH_3(g), absolute EtOH.

Scheme 27



	R	R_1	R_2
115	H	H	
116	H	Cl	
117	3-Me	H	
118	4-Me	H	
119	3-F	H	
120	4-Cl	H	
121	H	H	
122	2-Me	H	
123	3-Me	H	
124	3-F	H	
125	H	H	CH_2Ph
126	H	H	$(CH_2)_2PH$

(a) Method A: excess of R_2NH_2; (b) method B: R_2NH_2, Et_3N, absolute EtOH.

Scheme 28

	R_2
127	COMe
128	COPh
129	$COCH_2Ph$
130	CONHPh
131	$CONHCH_2Ph$

(a)RCOCl, pyridine, CH_2Cl_2; (b) $PhCH_2COOH$, 1-hydroxybenzotriazole, Et_3N(dimethylamino)pyridine, 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride, DMF; (c) RNCO, THF.

Scheme 29

Chart 1. Previously and Hereby Reported Adenosine Receptor Antagonists

A

B

97-106

107-131

R= H, Me, F, OMe, Cl
R_1=H, Cl

R_2=H, alkyl

R_2= H, cycloalkyl, aralkyl, acyl, carbamoyl

2,5-Dioxo-5,6-dihydropyrano[3,2-c]quinolines[102] were prepared by Junek <u>et</u> <u>al.</u>[102] They present a convenient synthesis for substituted 2,5-dioxo-5,6-dihydropyran[3,2-c]quinolines (**146_{a-p}**) in good yield by using the Knoevenagel reaction and cyclization in the presence of mild base. To synthesize pyrano[3,2-c]quinolines (**146_{a-p}**), 4-hydroxy-3-formylquinolin-2-ones (**144_{a-c}**) were considered as versatile bifunctional starting materials. **144_{a-c}** were prepared by adopting Riemer-Tieman reaction. 4-Hydroxy-3-formyl-1-methylquinolin-2-one (**144_a**) was treated with phenyl acetic acid in acetic anhydride in the presence of triethylamine at steam bath for 2h. After usual work up and purification, the corresponding 3-phenyl-6-methyl-2,5-dioxo-5,6-dihydropyrano[3,2-c]quinoline(**146_a**) was obtained. The other 4-hydroxy-3-formylquinolin-2(1H)-ones (**143_{a-c}**) were reacted similarly with a variety of active methylene compounds (**145_{a-f}**) to yield the corresponding 2,5-dioxo-5,6-dihydropyrano[3,2-c]quinolines (**146_{b-p}**). 6-Methyl-2,5-dioxo-5,6-dihydropyrano[3,2-c]quinoline (**146_q**) was obtained by Perkin reaction of **143_a** with acetic anhydride in the presence of anhydrous sodium acetate. The substituted pyrano[3,2-c]quinolines exhibited remarkable fluorescence.[103-104] The mechanism for the formation of **146_{a-p}** could involve, the carbanion derived from the active methylene compounds **145_{a-f}** may be considered to attack the carbonyl group without further interaction of base and the subsequent intramolecular ring closure lead to pyrano[3,2-c]quinolines.

143a-c → (i) → 144 → R_4O–C(=O)–CH_2–R_3 145a-e (ii) → 146a-q

(i) 15% NaOH / $CHCl_3$; (ii) Ac_2O / Base

Entry	R^1	R^2	R^3	R^4	Base
144$_a$	CH_3	H	-	-	-
144$_b$	C_6H_5	H	-	-	-
144$_c$	CH_3	Br	-	-	-
145$_a$	-	-	C_6H_5	H	-
145$_b$	-	-	p-$OCH_3C_6H_4$	H	-
145$_c$	-	-	$CO_2C_2H_5$	C_2H_5	-
145$_d$	-	-	$CONHC_6H_5$	H	-
145$_e$	-	-	$NHCOCH_3$	H	-
145$_f$	-	-	$COCH_3$	C_2H_5	-
145$_g$	-	-	H	CH_3CO	-
146$_a$	CH_3	H	C_6H_5	-	TEA
146$_b$	C_6H_5	H	C_6H_5	-	TEA
146$_c$	CH_3	Br	C_6H_5	-	TEA
146$_d$	CH_3	H	p-$OCH_3C_6H_4$	-	TEA
146$_e$	C_6H_5	H	p-$OCH_3C_6H_4$	-	TEA
146$_f$	CH_3	Br	p-$OCH_3C_6H_4$	-	TEA
146$_g$	CH_3	H	$CO_2C_2H_5$	-	TEA
164$_h$	C_6H_5	H	$CO_2C_2H_5$	-	TEA
146$_i$	CH_3	Br	$CO_2C_2H_5$	-	TEA
146$_j$	CH_3	H	$CONHC_6H_5$	-	TEA
146$_k$	C_6H_5	H	$CONHC_6H_5$	-	TEA
146$_l$	CH_3	Br	$CONHC_6H_5$	-	TEA
146$_m$	CH_3	H	$NHCOCH_3$	-	piperidine
146$_n$	C_6H_5	H	$NHCOCH_3$	-	piperidine
146$_o$	CH_3	Br	$NHCOCH_3$	-	piperidine
146$_p$	CH_3	H	$COCH_3$	-	piperidine
146$_q$	CH_3	H	H	-	NaOAc

Scheme 30

A number of ethyl 3H-pyrrolo[2,3-c]quinoline-2-carboxylates[105] have been prepared directly by condensation of ethyl azidoacetate with 4-formylquinolines, the procedure is based on the known thermal decomposition of α-azido acrylate bearing a β-aryl or heteroaryl substituent to give fused pyrroles. However, this method has been applied for the annulation of a pyrrole ring into a performed benzene,[106] thiophen,[107] furan[108] and indol ring[109] and no example dealing with annulation into quinoline ring. The key intermediate 4-formylquinolines **(150)** have been prepared from σ-(1-

methylethenyl)aniline[110] by sequential treatment with acid chlorides and phosphorous oxychloride[111] followed by oxidation with benzeneseleninic anhydride[112] of the resulting 4-methylquinolines **(149)**. Thus aniline derivative **147** reacts with acid chlorides in pyridine at 0°C leading to the corresponding amides **148** in excellent yields. When compounds **148** are treated with neat freshly distilled phosphorus oxychloride at reflux temperature, the corresponding 2-substituted 4-methylquinolines **(149)** are obtained. The oxidation of **149** into 4-formylquinolines is achieved by treatment with benzeneselenic anhydride in 1,2-dichlorobenzene. Treatment of compound **150** with ethyl azidoacetate in ethanol in presence of sodium ethoxide at -10 °C under nitrogen leads directly to 3H-pyrrolo[2,3-c]quinoline derivatives **(151)** (Scheme 31, 32).

148-151	R	148-151	R
a	4-MeOC_6H_4	d	Ph
b	4-ClC_6H_4	e	4-MeC_6H_4
c	4-pyridyl	f	4-O_2NC_6H_4

Scheme 31

Scheme 32

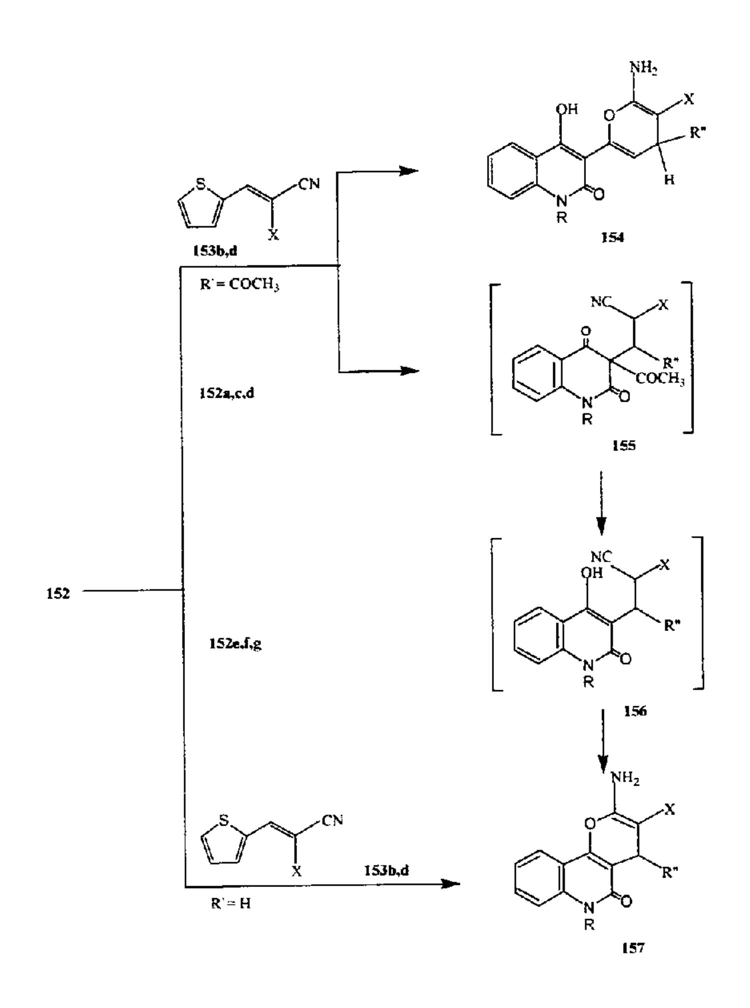
Several new 4H-pyran[3,2-c]quinolines[113-119] were prepared from the reaction of 4-hydroxy-2-(1H)quinolinones **(152)** and ylidenenitriles **(153)**. Compounds **160** were prepared from the reaction of 1-ethylidenemalononitrile **(153_e)** with **$152_{c,d}$** or **$152_{f,g}$**. Reaction of pyrano[3,2-c]quinoline **(161)** with **153_a** or **153_c** afforded benzo[b]pyrano[3,2-c]quinolines **(162 and 163)** respectively. Treatment of **$152_{b,c}$** with malononitrile and elemental sulfur yields **167**.

152a-f

152 a	R= H	R`= $COCH_3$	**152 b**	R= CH_3	R`= $COCH_3$
152 c	R= C_2H_5	R`= $COCH_3$	**152 d**	R= C_6H_5	R`= $COCH_3$
152 e	R= H	R`= H	**152 f**	R= C_2H_5	R`= H
152 g	R= C_6H_5	R`= H			

153a-d

153 a	R''= C_6H_5; X= CN	**153 b**	R''= 2-thienyl ; X= CN
153 c	R''= C_6H_5; X= $CO_2C_2H_5$	**153 d**	R''= 2-thienyl ; X=$CO_2C_2H_5$
152 e	R''= CH_3; X= CN		



157	R	R"	X
a	H	S	CN
b	C_2H_5	"	"
c	C_6H_5	"	"
d	H	"	$CO_2C_2H_5$
e	C_2H_5	"	"
f	C_6H_5	"	"

152c,d

158

159

153e

152f,g

160a,b

a	$R{=}C_2H_5$
b	$R{=}C_6H_5$

Scheme 33

Scheme 34

167_a R=CH_3
167_b R=C_2H_5

Scheme 35

Pyrano[3,2-f]quinolin-2(7H)-one and furo[3,2-h]quinolin-2-one was accomplished via a thermal[3,3]-sigmatropic rearrangement by Majumdar et al.[120]

The starting materials **170_{a-e}** were synthesized by treating 6-hydroxy-1-methylquinoline-2(H)-one **(168)** with different propynylic and allylic halides **(169)** in refluxing acetone in the presence of anhydrous potassium carbonate. A thermal [3,3]-sigmatropic rearrangement was utilized for the synthesis of the pyrano-and furano-quinolines. The pyrano[3,2-f]quinolin-2(7H)-ones **(171a,b)** were obtained by heating the propynyl ethers **170a,b** in refluxing N,N-diethylaniline.

HO 168 + R—X 169 → RO 170

	X	R		X	R
a:	Br	$CH_2C \equiv CH$	d:	Br	$CH_2CH=CH_2$
b:	Br	$CHMeC \equiv CH$	e:	Br	$CH_2CH=CHMe$
c:	Br	$CH_2C(Cl)=CH_2$			

Scheme 36

170a,b → 171a,b

a: $R^1 = H$
b: $R^1 = Me$

Scheme 37

The formation of pyrano[3,2-f]quinoline-2(7H)-ones **($171_{a,b}$)** may be rationalized by the initial [3,3]-sigmatropic rearrangement of the propynyl ethers **$170_{a,b}$** to the allenyl derivatives **172** followed by enolization, [1,5]-hydrogen shift, and electrocyclic ring clouser[121] to give the products **$171_{a,b}$.**

170a,b → [3,3] → 172 ⇌ 173 → [1,5]H shift → 174 → ECR → 171a,b

Scheme 38

The furo[3,2-f]quinolin-2-one derivatives **176** and **178** were synthesized via two different routes. In one rout, the chloropropenyl ether **170_c** was heated in refluxing N,N-diethylaniline for 12h to give the corresponding chlorallyl enol **175** which was easily cyclized to the corresponding 1,6-dimethylfuro[3,2-f]quinolin-2-one **176** in 80 % yield when treated with 20 % alcoholic KOH for 3h. (Scheme 39).

170c → 175 (HO, Cl) → 176

Scheme 39

170d,e → 177d,e (HO, H, R^2) → 178 (R^2)

177_d R^2=H
177_e R^2=Me

Scheme 40

Ghorab et al[122] reported that 2-alkyl(or aryl)-12-(2-bromophenyl)-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinolines of potential biochemical activity have been synthesized.

Scheme 41

The starting material, 2-amino-4-(2-bromophenyl))-5,6,7,8-tetrahydroquinoline-3-carbonitrile **(183)** was synthesized by the reaction of 2-bromobenzaldehyde **(179)**, malononitrile and cyclohexanone **(180)** in equimolar proportions in the presence of ammonium acetate. The formation of 2-amino-4-(2-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile **(183)** was rationalized in terms of the initial formation of benzylidenemalononitrile **(181)** followed by the addition of cyclohexanone to the ylidenic bond forming acyclic intermediate **182**. Amination of **182** in the presence of ammonium acetate followed by cyclization of the

enamine and partial dehydrogenation under the reaction conditions afforded the final product **183** (Scheme 41). This was confirmed through equimolar condensation of **181** and **180** under the previous conditions, which also afforded **183**.

Treatment of **183** with triethyl orthoformate gave 2-ethoxymethylenamino-4-(2-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile **(184)**, which reacted with hydrazine hydrate at room temperature to yield the 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-3-amine **(185)**.

A combination of the pyrimidinoquinoline system with a triazole moiety was afforded through the condensation of 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-3-amine **185** with various acid chloride and ester derivatives.

Treatment of compound **185** with chloroacetyl chloride and / or ethyl cyanoacetate yielded the corresponding 12-(2-bromophenyl)-2-chloromethyl-8,9,10,11-tetrahydro-[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline **(188)** and 12-(2-bromophenyl)-2-cyanomethyl-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline **(189)** respectively, while with carbon disulphide, the 12-(2-bromophenyl)-2-thioxo-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline **(191)** was obtained.

Condensation of **185** with ethyl chloroformate afforded ethyl 12-(2-bromophenyl)-2-oxo-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline-3-carboxylate **(193)**.

When **185** was refluxed with triethyl orthoformate or formic acid, it afforded the corresponding 12-(2-bromophenyl)-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]-pyrimido[4,5-b]quinoline **(186)**, whereas with acetic anhydride or benzoyl chloride, the respective 12-(2-bromophenyl)-2-methyl-8,9,10,11-tetrahydro[1,2,4]triazolo-[5',1':6,1]pyrimido[4,5-b]quinoline **(187)** and 12-(2-bromophenyl)-2-phenyl-8,9,10,11-tetrahydro[1,2,4]triazolo[5',1':6,1]pyrimido[4,5-b]quinoline **(190)**, were obtained.

Reaction of 5-(2-bromophenyl)-4-imino-6,7,8,9-tetrahydro-pyrimido[4,5-b]-quinoline-3-amine **(185)** with ethyl chloroacetate in refluxing sodium methoxide solution yielded the triazinopyrimidoquinoline derivative **195** rather than its isomeric structure **194** (Scheme 42). Structure **195** was suggested rather than structure **194**, based on assumption that the reaction basic condition allowed it to proceed through formation of sodium salt on the less basic imino nitrogen atom, and elimination of

sodium chloride followed by cyclization 192. In addition, the IR spectrum of the isolated product showed a carbonyl band at 1660 cm^{-1}, which was at less frequency than that expected for structure **194**. Further evidence was the ^{1}H-NMR spectrum which showed a singlet at 4.3 ppm for the methylene protons.

Ar = 2-Br-C_6H_4

Scheme 42

Interaction of compound **185** with diethyl oxalate gave a triazolopyrimidoquinoline derivative **198**. This was confirmed by its elemental analysis, ^{1}H-NMR and mass spectra. These results are in agreement with the method previously reported **195**.

Biochemical screening of some of the synthesized compounds revealed that quinoline derivative **184** showed a significant increase in SGPT and SGOT activities. On the other hand, triazinopyrimidoquinoline derivative **195** significantly decreased serum creatinine.

Barret[123] reported the synthesis of new tetracyclic compounds **204** and studied the relation between the substitution of the aromatic substituent and the cytotoxic activity.

Some analogs **202** of amsacrine[124] **201** with a tetracyclic quinoline structure and an amine moiety R as a side chain, have been synthesized.[125] These authors have shown that the cytotoxic activity is dependant upon R and X. The best activity was obtained when X was a methylene group, an oxygen or a sulfur atom and R an arylamino group bearing an electron-withdrawing substituent such as $NHSO_2CH_3$. These compounds are active against KB-cells (in vitro and in vivo), P388 leukemia and various solid tumors.[126]

201 202

Chang has synthesized indolo[3,2-b]quinolines[127] **(203)**. These compounds are cytotoxic against leukemia P388 in mice, in particular when R is a galactopyranosyl moiety.

203 204

In this work he has synthesized new tetracyclic compounds **204** and studied the relation between the substitution of the aromatic substituent and the cytotoxic activity.

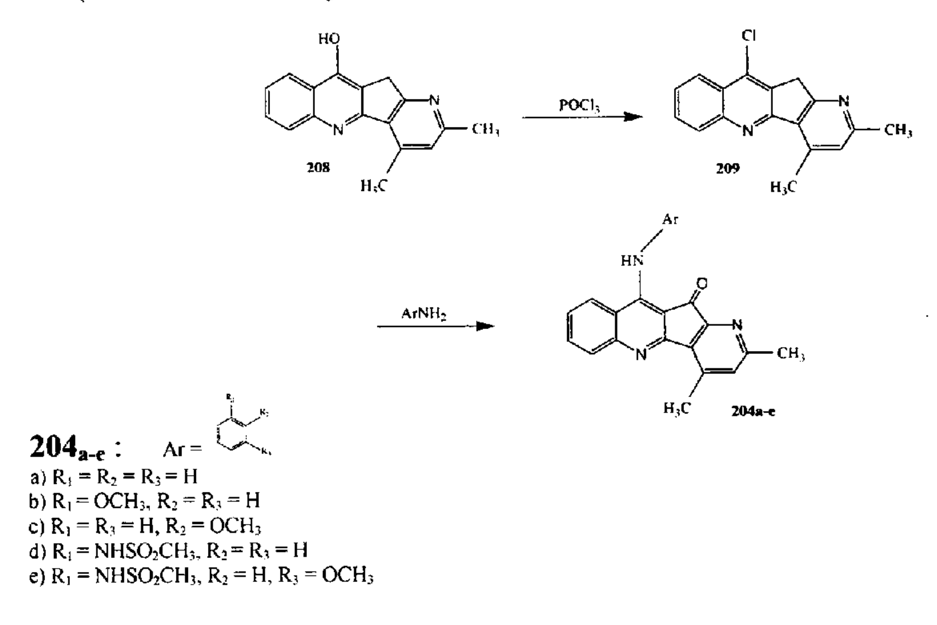
The 5-oxo-2,4-dimethyltetrahydroquinoline[128] **(205)** was reacted with phenylhydrazine (Fisher reaction) to give the tetracyclic compound **206** , which led to the ketolactam **207** by either ozonolysis or periodate oxidation. Compound **208** was obtained by cyclization in alkaline medium.[129] Compound **206** is unstable and must be

used immediately after preparation. It is quickly oxidized to a 5,6-dehydrogenation product (Scheme 43).

$C_6H_5NH\text{-}NH_2$, CH_3COOH
205 → 206
$NaIO_4$, MeOH, H_2O or O_3, CH_3Cl
207 → NaOH → 208

Scheme 43

The chloro derivative **209** was obtained by treatment of **208** with phosphoryl chloride (Scheme44). At this point, different amines were condensed with **209**. Stirring **209** at room temperature with the appropriate amine in methanol afforded **204** after 15 days in low yield. Heating of these solutions at a reflux temperature led only to degradation products. Other procedures such as stirring the solution of **209** and amines in N-methyl-2-pyrrolidinone,[130a] heating at 100 °C in phenol in the absence[130b] or in the presence of potassium iodide[130c] or at reflux in ethanol,[130d] did not give the expected products. Finally, improvement was obtained by the use of Andersen's process (reflux in 2-methoxyethanol instead of 2-ethoxyethanol). [131]



Scheme 44

New spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinonline)]-2,4'-dione[132] (**216**$_{a-e}$) derivatives were prepared according to the following:

a: R = H
b: R = CH_3
c: R = OCH_3
d: R = Cl
e R = Br

Scheme 45

Reaction of compounds **213a-e** with triflic acid yielded the target cyclodehydration products; spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinoline)]-2,4'-dione derivatives **215a-e** (Scheme 46). Alkylation of compounds **213**$_{a-e}$ with methyl iodide and anhydrous potassium carbonate in dry acetone afforded 3-arylmethylamino-3-(1-methyl-2-oxoindole) acetic acid derivatives **214a-e** in good yield. The reaction of compounds **214a-e** with trifilic acid yielded spiro[indoline-3,2'-(1',2',3',4'-tetrahydroquinoline)]-1,1'-dimethyl-2,4'-dione derivatives **216**$_{a-e}$ in good yields (Scheme 46). For the rigid identification of compounds **216a-e**, unequivocal syntheses for **216**$_{a-e}$ were established by the alkylation of compounds **215a-e** with methyl iodide.

213_{a-e}-216_{a-e}

a: R = H
b: R = CH_3
c: R = OCH_3
d: R = Cl
e: R = Br

Scheme 46

Results and Discussion

RESULTS AND DISCUSSION

The pyran ring system is an interesting class of heterocycles. It has been reported that pyran derivatives exhibit antimicrobial activities,[133] growth stimulating effects,[40] antifungal and plant growth regulation effects,[37] antitumor activity,[38]central nervous system activity[45] and hypotensive[44] effect. On the other hand, fused pyrimidines were found to possess a wide biological activities such as antimicrobial[49]antiparkinsonion[51] leishmanicidal and herbicidal.[55] Moreover, quinoline derivatives have found useful applications as antimicrobial,[133] antimalarial,[135] cardiovascular and biochemically active compounds.[136] In addition to the previously mentioned properties, many imidazoles and triazines are used as therapeutic tools.[62,63,81] Based on these findings, it was of interest to introduce these biologically active moieties in one molecule, giving rise to a new series of potentially biochemically active compounds.

It has been found that 5-choloro-8-quinolinol **(217)** reacts with the ylidenenitriles in ethanol and in the presence of catalytic amount of piperidine for which two products **$218_{a\text{-}e}$-$219_{a\text{-}e}$** and **$218'_{a\text{-}e}$-$219'_{a\text{-}e}$** seemed possible.[113, 137-140] Structures **$218_{a\text{-}e}$-$219_{a\text{-}e}$** were established for the reaction products based on ^{1}H-NMR spectra which revealed the presence of a 4H-pyran proton at δ=4.80-5.10 ppm, thus structures **$218'_{a\text{-}e}$-$219'_{a\text{-}e}$** were readily ruled out[137,138] (Scheme 47).

Cl, OH, N — 217 + Ar—HC=C(CN)X → 218a-e-219a-e (Cl, H, Ar, X, NH₂, O, N); ↛ 218'a-e-219'a-e (Cl, NH₂, X, Ar, H, O, N)

X=COOEt, CN

218a-e: X=CN

$219_{a\text{-}e}$: X=COOEt

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) 2-furyl, e) 2-thienyl

Scheme 47

The structures of compounds **218_{a-e}** **-219_{a-e}** namely 2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines and Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]-quinoline-3-carboxylates, respectively were established from their elemental analysis and spectroscopic data. The IR (KBr, ν cm^{-1}) spectrum showed the absorptions bands at 3324-3180 (NH_2), 2192 (CN) for compound **218_a** and at 3473-3273 (NH_2), 1731 (CO) for compound **219_a**. The ^1H-NMR ($CDCl_3$, δ ppm) spectrum showed the following signals: 4.90 (1H, s, pyran ring), 8.80 (2H, s, NH_2) and 6.90-8.10 (9H, m, arom.) for compound **218_a** and at 5.10 (1H, s, pyran ring), 1.30 (3H, t, CH_3), 4.20 (2H, q, CH_2), 8.90 (2H, s, NH_2) and 7.80-8.50 (9H, m, arom.) for compound **219_a** (cf. fig. 3).

Compounds **218_{a-e}** proved to be a useful key intermediate in the synthesis of fused heterocyclic systems. Thus the pyrimido[4',5':6,5]pyrano[3,2-h]quinolines **(220_{a-e}** **-** **222_{a-e})** were produced when compounds **218_{a-e}** were reacted with acetic anhydride / pyridine mixture, formamide and formamide/formic acid mixture respectively.

The IR (KBr, ν cm^{-1}) spectrum showed the absorption bands at 3391 (NH), 1690 (CO) for **220_a** ; 3440-3340 (NH_2) for **221_a** and 3100 (NH), 1690 (CO) for **222_a** respectively (Scheme 48).

Cl
Ar
N
O
O
N NH
222a-e
$HCONH_2$
HCOOH
221a-e: Cl, Ar, N, O, NH_2, N N
$HCONH_2$
218a-e: Cl, Ar, N, O, CN, NH_2
Ac_2O
Pyridine
220a-e: Cl, Ar, N, O, O, N NH, CH_3

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [2-furyl] , e) [2-thienyl]

Scheme 48

4-Aryl-3-cyano-6-chloro-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]quinolines (**$223_{a\text{-}e}$**) were obtained by refluxing compounds **$218_{a\text{-}e}$** with triethylorthoformate. The IR spectrum of compound **223_a** showed band at 2208 cm^{-1} due to the cyano group with the disappearance of the characteristic band due to the amino group. The ^{1}H-NMR spectrum ($CDCl_3$, δ ppm) shows a new triplet at 1.65 ppm and quartet at 4.20 ppm, which are assigned to CH_3 and CH_2 of the ethoxy group beside the expected signals of the rest of the molecule (Scheme 49).

Cl Ar N O CN NH2 218a-e — HC(OEt)3 → Cl Ar N O CN N 223a-e OEt

Ar= a) C_6H_5, b) p-$OCH_3C_6H_4$, C) p-$NO_2C_6H_4$, d) [2-furyl], e) [2-thienyl]

Scheme 49

Compounds **$223_{a\text{-}e}$** underwent aminolysis and cyclization by treatment with aniline to give in "one step reaction" 7-aryl-5-chloro-8-imino-9-phenylpyrimido[4',5':6,5]-pyrano[3,2-h]quinolines (**$224_{a\text{-}e}$**). The ^{1}H-NMR data (absence of signals due to ethoxy group) support the formation of these compounds.

The interaction of **$218_{a\text{-}e}$** with ethyl cyanoacetate led to the formation of 8-amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano[3,2-h]quinolines (**$225_{a\text{-}e}$**). The structure was established by elemental analyses and spectral data such as the appearance of new characteristic absorption bands in the IR spectrum at 3334-3201 cm^{-1} and 2203 cm^{-1} attributable to the amino and cyano groups respectively.

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [furyl], e) [thienyl]

Scheme 50

The [1]H-NMR (CF_3COOD, δ ppm) spectrum of **225_{a-e}** showed signals at 4.95 (1H, s, pyran) and 7.00-8.10 (9H, m, arom.). Furthermore, compounds **218_{a-e}** gave the corresponding triazine derivatives **226_{a-e}** by means of diazotization with sodium nitrite in a mixture of hydrochloric and acetic acid (Scheme 50); all compounds were identified by conventional methods such as elemental and spectral analyses. The IR spectrum showed the disappearance of absorption bands due to the amino and cyano groups.

2-Amino-4-aryl-3(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]quinolines **(227_{a-e})** were prepared by the reaction of the pyranoquinolines **218_{a-e}** with ethylendiamine (Scheme 51).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [furyl], e) [thienyl]

Scheme 51

The structure of compounds 227_{a-e} were confirmed by their elemental analyses and spectral data (cf. experimental section). The IR spectrum showed a new absorption band at 3437 cm^{-1} due to NH and the ^{1}H-NMR spectrum showed a new signal as a singlet at 8.95 ppm due to NH proton and two triplets at 3.30, 3.90 ppm which are assigned to imidazolyl-H atoms, beside the absorption bands and signals of the rest of the molecule. Compounds 227_{a-e} serve as intermediate for the synthesis of imidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines. Thus the cyclization of compounds 227_{a-e} with triethyl orthoformate, aldehydes and ketones gave the corresponding 2,3-dihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**228_{a-e}**) and 2,3,5,6-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**229_{a-e}-230_{a-e}**) while the reaction with cyclic ketones and carbon disulfide gave spiroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**231_{a-e}-232_{a-e}**) and 5-thioxo-2,3,6-trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (**233_{a-e}**) respectively (Scheme 52).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [furyl], e) [thienyl]

Scheme 52

The structures of compounds **228_{a-e}-233_{a-e}** were confirmed by their elemental analysis and spectral data (cf. experimental section). Compounds **228_{a-e}** clearly follow from disappearance of the NH_2 and NH bands in the IR and ^{1}H-NMR spectra and the appearance of the expected side chain signals in the ^{1}H-NMR spectra of compounds **229_{a-e}-232_{a-e}** (for more details cf. experimental section).

Interaction of compounds **218_{a-e}** with nitrous acid gave the corresponding 5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines **(226_{a-e})**. The structures **226_{a-e}** clearly follow from disappearance the amino group bands in the IR spectra.

Triazines are used as cardiotonic agents,[83] fungicide,[73] herbicides,[81] blood platelet antiagregation,[82] antipsychotic agent,[77] and antimicrobial activity.[80] This high biological and pharmacological important of triazines and fused triazino heterocycles prompted us to synthesize 5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino-[4',5':6,5]pyrano[3,2-h]quinolines **(234a-e)**.

The chlorine atom reactivity at C-4 of compounds **226_{a-e}** was highlighted by its easy displacement with nucleophilic reagents as hydrazine hydrate to give the hydrazino derivatives **234_{a-e}** which in turn, proved to be a useful intermediate (Scheme 53).

218a-e —($NaNO_2$ / HCl)→ 226a-e —(N_2H_4)→ 234a-e

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 53

The structures of compounds **234_{a-e}** were confirmed by elemental analysis, IR and ^{1}H-NMR spectra. The IR (KBr, ν cm^{-1}) spectrum of compound **234_a** showed absorption bands at 3473 (NH), 3324-3181 (NH_2). The ^{1}H-NMR ($CDCl_3$, δ ppm) showed the following signals: 4.30 (2H, s, NH_2), 5.00 (1H, s , pyran ring), 7.00-8.60 (9H, m, arom.) and 8.90 (1H, s, NH).

In fact, 14-aryl-12-chloro[1,2,4]triazolo[3",4"-f][1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines **(235_{a-e})** and 14-aryl-12-chloro-3-thioxo[1,2,4]triazolo[3",4"-f][1,2,3]-triazino[4',5':6,5]pyrano[3,2-h]quinolines **(236_{a-e})** were produced from the reaction of

compounds **234_{a-e}** with formic acid and carbon disulfide respectively (cf. experimental section).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 54

The formation of compounds **235_{a-e}** - **236_{a-e}** were clearly obvious by the examination of their IR spectrum which revealed the absence of NH_2 and NH bands in compounds **235_{a-e}** and the presence of NH and CS bands in compounds **236_{a-e}**. The ^{1}H-NMR ($CDCl_3$, δ ppm) of compound **235_a** and **236_a** (CF_3COOD, δ ppm) showed the following signals: 5.00 (1H, s, pyran ring), 6.60 (1H, s, triazolo), 7.10-8.60 (9H, m, arom.) and 5.00 (1H, s, pyran ring), 7.00-8.50 (9H, m, arom.)respectively.

In addition, treatment of **234_{a-e}** in acetic acid and an aqueous solution of sodium nitrite at room temperature gave one of the two structures showed in (Scheme 55).

One of them is in agreement with the IR spectrum which revealed the appearance of a band characteristic to the azido group, so, this structure is 5-aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines **(237_{a-e})** and ruling out the alternative tetrazolo structures **$237'_{a-e}$** (Scheme 55).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 55

Recent years have witnessed the synthesis and characterization of a number of nitrogen-containing hetero aromatics. In fact, the biological activities of these compounds have drawn the attention of organic chemist for a long time. The synthesis of pyranoquinoline derivatives has gained very important goals to be used as antimicrobial activity.[120, 134, 138-140] The pyrrolopyrazine derivatives were reported by Robba and his colleagues.[141-145] We presently involved in a program directed to the synthesis of pyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h]quinoline derivatives and related hexacyclic heterocycles.

The amino function of ethyl 2-amino-4-aryl-6-chloro-4*H*-pyrano[3,2-h]quinoline-3-carboxylates (**219_{a-e}**) were easily converted to the corresponding 1-pyrrolyl group via the interaction with 2,5-dimethoxytetrahydro furan in boiling acetic acid to give ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4*H*-pyrano[3,2-h]quinoline-3-carboxylates (**238_{a-e}**) (Scheme 56).

Ar= a) C_6H_5, b) p-$OCH_3C_6H_4$, C) p-$NO_2C_6H_4$, d) , e)

Scheme 56

The structures of compounds **238_{a-e}** were conformed by elemental analysis and spectral data. The IR (KBr, ν cm^{-1}) showed the disappearance of the amino group band due to the formation of pyrrolyl ring . The ^{1}H-NMR ($CDCl_3$, δ ppm) showed a new signals at 6.40-6.75 ppm which is assigned to the pyrrolyl-H atoms. For instance for compound **238_a**: 1.38 (3H, t, CH_3), 4.30 (2H, q, CH_2), 5.10 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.75 (2H, m, pyrrolyl ring), 7.10-8.60 (9H, m, arom.).

The latter pyrrolyl ester was reacted with hydrazine hydrate to give the pyrrolyl hydrazide **239_{a-e}** which indicated by the appearance of characteristic band of hydrazide group on its IR spectrum. The ^{1}H-NMR (CF_3COOD, δ ppm) of compound **239_a** showed the following signals: 5.00 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.70 (2H, m, pyrrolyl ring), 7.10-8.60 (9H, m, arom.) (Scheme 57).

Cl, N, O, N, Ar, COOEt — **238a-e** —(N_2H_4)→ Cl, N, O, N, Ar, $CONHNH_2$ — **239a-e**

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) (2-furyl), e) (2-thienyl)

Scheme 57

2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano-[3,2-h]quinolines **(240_{a-e})** were the product of the reaction between the hydrazides **239_{a-e}** and acetylacetone . The IR (KBr, ν cm^{-1}) spectrum **240_a** showed characteristic bands at 1700 cm^{-1} due to CO and at 1603 cm^{-1} due to C=N. The ^{1}H-NMR ($CDCl_3$, δ ppm) spectrum of **240_a** showed the expected signal pattern at: 1.80 (6H, s, $2CH_3$), 5.00 (1H, s, pyran ring), 6.30 (2H, m , pyrrolyl ring), 6.50 (2H, m, pyrrolyl ring), 7.10-8.50 (9H, m, arom.) (Scheme 58).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [furyl], e) [thienyl]

Scheme 58

The treatment of the hydrazide $\mathbf{239_{a\text{-}e}}$ with nitrous acid gave the corresponding 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-oylazides ($\mathbf{241_{a\text{-}e}}$). The structure of compound $\mathbf{241_a}$ was established by IR (appearance of a new band at 2213 cm^{-1} due to the azide group) and ^{1}H-NMR spectra which showed the expected signals at: 5.10 (1H, s, pyran ring), 6.40 (2H, m, pyrrolyl ring), 6.60 (2H, m, pyrrolyl ring), 7.30-8.60 (9H, m, arom.) (cf. the experimental section).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) [furyl], e) [thienyl]

Scheme 59

The acid azide is a versatile compound and could be transformed into a variety of derivatives. When $\mathbf{241_{a\text{-}e}}$ were heated in boiling ethanol, the ethylcarbamate $\mathbf{242_{a\text{-}e}}$ were obtained. When they reacted with hydrazine hydrate, the products were the semicarbazides $\mathbf{243_{a\text{-}e}}$ (Scheme 60).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 60

The structures of compounds $\mathbf{242}_{a\text{-}e}$ - $\mathbf{243}$-$_{a\text{-}e}$ were confirmed by their analytical and spectral data. The IR ((KBr, ν cm^{-1}) spectrum showed characteristic bands at 3375 (NH), 1707 (CO) for compound $\mathbf{242}_a$ and at 3447 (NH), 3350-3160 (NH_2), 1700 (CO) for compound $\mathbf{243}_a$. The ^{1}H-NMR (CF_3COOD) showed the following signals: 2.10 (3H, t, CH_3), 4.20 (2H, q, CH_2), 5.10 (1H, s, pyran ring), 6.30 (2H, m, pyrrolyl ring), 6.60 (2H, m, pyrrolyl ring), 7.30-8.50 (9H, m, arom.) for compound $\mathbf{242}_a$ and at 5.10 (1H, s, pyran ring), 6.20-8.30 (13H, m, arom.) for compound $\mathbf{243}_a$ respectively.

Heating the acid azides $\mathbf{241}_{a\text{-}e}$ in a high-boiling point inert solvent such as xylene led to Curtius rearrangement with concomitant ring closure of the isocyanate intermediate $\mathbf{241'}_{a\text{-}e}$ giving 7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1",2":1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinolines **($\mathbf{244}_{a\text{-}e}$)**. The formation of $\mathbf{244}_{a\text{-}e}$ are due to the high reactivity of the isocyanate intermediate which could not be isolated under the

reaction conditions used. The structure of compound **244_a** was established by IR (absence of NH_2 band), Mass and ^{1}H-NMR spectra.

The latter oxo compounds **244_{a-e}** could be transformed into the corresponding chloro derivatives namely 7-Aryl-5,9-dichloropyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano-[3,2-h]quinolines **(245_{a-e})** when heated under reflux with phosphoryl chloride. The structures **245_{a-e}** clearly follow from disappearance the NH bands in the IR and ^{1}H-NMR spectra and the appearance of the expected signals of the rest of the molecules in the ^{1}H-NMR spectra (Scheme 61).

Phosphoryl chloride

244a-e 245a-e

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 61

The reactivity of the chlorine atom at C-9 of **245_{a-e}** was shown by its easy displacement using various nucleophilic reagents such as hydrazine hydrate to give 7-Aryl-5-chloro-9-hydrazinopyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines **(246_{a-e})** (Scheme 62).

N_2H_4

245a-e 246a-e

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 62

The hydrazino derivatives **246_{a-e}** proved to be a useful compound for synthetics. The triazolo derivatives **247_{a-e}** and **248_{a-e}** were produced from the reaction of **246_{a-e}** with acetic acid and carbon disulfide respectively (Scheme 63).

Ar = a) C_6H_5, b) p-$OCH_3C_6H_4$, c) p-$NO_2C_6H_4$, d) , e)

Scheme 63

The structures of compounds **247_{a-e}** and **248_{a-e}** were confirmed by elemental analysis, IR, ^{1}H-NMR and MS spectroscopy. The IR ((KBr, ν cm^{-1}) spectrum of **247_a** showed the disappearance of NH band and the ^{1}H-NMR ($CDCl_3$, δ ppm) showed a new singlet at 2.10 ppm which is assigned to the methyl group.

Antibacterial Activity

The antibacterial activity of the synthesized compounds was tested against *Escherichia coli* and *Staphylococcus aureus* using the agar cup diffusion technique[146] and results of the biological testing are given in Table 1. The data showed that most of the newly synthesized compounds exhibited remarkable effects.

Antifungal activity

The newly synthesized compounds were screened for their antifungal activity against three species of fungi, namely, *Aspergillus flavus*, *Aspergillus niger* and *Penicillium chrysogenum*, using the disk diffusion method.[147-148] The tested compounds were dissolved in N,N-dimethylformamide (DMF) to get a solution of 1% concentration. Filter paper discs (Whatman, 5 mm diameter) were saturated with this former solution. The saturated filter paper discs were placed on the surface of solidified Czapek's Dox agar dishes seeded by the test fungi. The inhibition zones were measured in mm at the end of an incubation period of 48h at 28 °C and 8-quinolinol was used as standard reference. As appear in Table 2, compounds $\mathbf{238}_{a\text{-}c}$, $\mathbf{239}_{a}$, $\mathbf{240}_{a\text{-}c}$, $\mathbf{241}_{a}$, $\mathbf{241}_{c}$, $\mathbf{243}_{a\text{-}b}$, $\mathbf{244}_{a\text{-}b}$, $\mathbf{245}_{a\text{-}c}$, $\mathbf{246}_{c}$ and $\mathbf{248}_{a\text{-}c}$ exhibited strong activity (inhibition zones ranged from 25-40 mm). Compounds $\mathbf{238}_{d\text{-}e}$, $\mathbf{239}_{b\text{-}c}$, $\mathbf{240}_{d\text{-}e}$, $\mathbf{241}_{b}$, $\mathbf{242}_{a\text{-}b}$, $\mathbf{243}_{c\text{-}e}$, $\mathbf{244}_{c}$, $\mathbf{245}_{d\text{-}e}$, $\mathbf{246}_{a\text{-}b}$,$\mathbf{246}_{d\text{-}e}$ showed moderate activity (inhibition zones ranging from 11-20 mm). On the other hand, compounds $\mathbf{239}_{d\text{-}e}$, $\mathbf{241}_{d\text{-}e}$, $\mathbf{242}_{c\text{-}e}$, $\mathbf{244}_{d\text{-}e}$, $\mathbf{247}_{a\text{-}e}$ and $\mathbf{248}_{d\text{-}e}$ showed weak activity (inhibition zones ranged from 3-9 mm) in comparison to the standard.

Table1: Antimicrobial screening of compounds (**218_{a-e}–236_{a-e}**) (inhibition zones mm)

Compd. No.	*Escherichia coli*	*Staphylococcus aureus*	Compd. No.	*Escherichia coli*	*Staphylococcus aureus*
218a	22	16	224e	25	33
b	28	23	225a	31	32
c	21	19	b	24	35
d	33	22	c	21	15
e	44	27	d	23	20
220a	23	26	e	31	19
b	28	31	226a	20	21
c	-	19	b	26	17
d	23	19	c	-	28
e	36	22	d	19	21
221a	22	18	e	26	32
b	18	25	227a	20	29
c	21	21	b	33	35
d	16	16	c	19	-
e	29	34	d	17	21
222a	20	-	e	36	50
b	19	21	228a	22	31
c	23	18	b	37	27
d	-	18	c	26	19
e	19	-	d	23	28
223a	18	18	e	42	57
b	26	26	229a	18	21
c	-	-	b	23	19
d	19	19	c	18	24
e	36	29	d	-	16
224a	22	24	e	22	-
b	21	23	230a	24	33
c	23	15	b	40	29
d	21	19	c	14	22

Table 1 (contin.)

230d	27	31	233e	33	39
e	44	61	234a	21	25
231a	19	21	b	36	22
b	25	19	c	22	32
c	23	-	d	25	23
d	26	23	e	31	28
e	24	31	235a	-	21
232a	277	36	b	29	-
b	43	32	c	-	19
c	25	16	d	18	-
d	31	34	e	24	21
e	47	29	236a	31	36
233a	22	26	b	45	31
b	35	24	c	30	38
c	-	29	d	44	32
d	22	25	e	39	46
Tetracycline	12	15	Tetracycline	12	15

Table 2: Antifungal activity of tricyclic heterocyclic quinoline derivatives (**238_{a-e}-248_{a-e}**).

Inhibition of spore germination							
Compd. No.	*Aspergillus flavus*	*Aspergillus niger*	*Penicillium chrysogenum*	Compd. No.	*Aspergillus flavus*	*Aspergillus niger*	*Penicillium chrysogenum*
238a	25	32	23	243d	17	15	16
b	30	24	26	e	18	15	13
c	29	27	22	244a	40	36	31
d	14	17	15	b	36	28	37
e	12	15	13	c	19	13	15
239a	33	28	26	d	8	7	6
b	11	14	14	e	6	4	8
c	13	16	14	245a	35	31	26
d	6	4	10	b	29	23	21
e	9	6	8	c	31	28	25
240a	26	31	22	d	15	17	20
b	29	25	27	e	12	13	11
c	31	29	24	246a	14	11	14
d	15	18	16	b	13	16	18
e	14	16	13	c	34	28	31
241a	28	24	33	d	11	14	12
b	17	15	13	e	13	12	10
c	25	21	26	247a	8	5	6
d	8	6	9	b	8	8	6
e	9	8	11	c	7	9	10
242a	13	16	18	d	5	6	5
b	17	12	14	e	9	4	7
c	9	7	11	248a	38	40	33
d	6	8	4	b	31	36	26
e	3	5	6	c	34	27	29
243a	33	29	26	d	9	10	11
b	27	24	31	e	6	8	4
c	14	19	17	8-quinolinol	9	10	12

Experimental

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The time required for completion of each reaction was monitored by TLC. IR ($\nu.cm^{-1}$) spectra were recorded on a Nicolet Jeol technique in the range of 4000-400 cm^{-1} 205 FTIR with KBr. ^{1}H-NMR (δ, ppm) spectra were recorded on an EM-360 90-MHz spectrometer using TMS as internal standard. ^{13}C-NMR (δ, ppm) were measured on a varian FT-80 spectrophotometer. Elemental analysis was determined on a Perkin Elmer 240 C microanalyser. Mass spectra were recorded on Jeol JMS 600 instrument (Assiut university).

2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines (218_{a-e}).

General procedure: A mixture of arylidenemalononitrile (0.01 mol) and 5-chloro-8-quinolinol **(217)** (0.01 mol) was heated under reflux in absolute ethanol (50 ml) using a catalytic amount of piperidine for 6h. The solvent was evaporated under reduced pressure, cooled and poured into ice cold water. The solid products were collected, washed several times with water and recrystallized from ethanol.

a: Yellowish brown crystals (68% yield), mp. 123 °C.

Analysis of $C_{19}H_{12}N_3OCl$ (333.82). Calcd. %: C, 68.36; H, 3.62; N, 12.59; Cl, 10.64; Found %: C, 68.47; H, 3.69; N, 12.48; Cl, 10.70

IR: 2192 (CN), 3324-3180 (NH_2), 3057 (CH arom.), 2924-2858 (CH aliph.) (fig.2). MS, m/z: 333.76 (fig.3).

^{1}H-NMR ($CDCl_3$): 4.90 (1H,s), 8.8 (2H,s), 6.90-8.10 (9H,m). (fig.3)

^{13}C- NMR: 158.86, 148.34, 133.44, 129.18, 127.44, 126.81, 122.56, 115.09, 111.79, 92.13, 77.30, 76.67, 55.77.

b: Pale yellow crystals (73% yield), mp. 73 °C.

Analysis of $C_{20}H_{14}N_3O_2Cl$ (363.84). Calcd. %: C, 66.02; H, 3.88; N, 11.55; Cl, 9.76. Found %: C, 66.17; H, 3.91; N, 11.64; Cl, 9.81.

IR: 2192 (CN), 3390-3190 (NH_2), 2837 (CH aliph.) (fig.4). MS, m/z: 363.60

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.20 (3H, s), 6.90-8.10 (8H, m), 8.15 (2H, s).

c: Pale brown crystals (77% yields), mp. 82 °C.

Analysis of $C_{19}H_{11}N_4O_3Cl$ (378.82). Calcd. %: C, 60.24; H, 2.93; N, 14.79; Cl, 9.37. Found %: C, 60.37; H, 2.89; N, 14.66; Cl, 9.44.
IR: 2182 (CN), 3318-3062 (NH_2) (fig.6). MS, m/z: 378.81 (fig.7).
^{1}H-NMR ($CDCl_3$): 4.90 (1H, s), 6.90-8.10 (8H, m), 8.15 (2H, s) (fig.7).

d: Dark brown crystals (85% yields), mp. 117 °C.
Analysis of $C_{17}H_{10}N_3O_2Cl$: (323.78). Calcd. %: C, 63.06; H, 3.11; N, 12.98; Cl, 10.96. Found %: C, 63.22; H, 3.16; N, 12.20; Cl, 10.84.
IR: 2217 (CN), 3324-3196 (NH_2). MS, m/z: 323.84 (fig. 8).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.70-8.00 (7H, m), 8.10 (2H, s).

e: Dark brown crystals (82% yields), mp. 111 °C.
Analysis of $C_{17}H_{10}N_3OSCl$ (339.88). Calcd. %: C, 60.07; H, 2.97; N, 12.37; S, 9.45; Cl, 10.45. Found%: C, 60.24; H, 2.89; N, 12.46; S, 9.54; Cl, 10.55.
IR: 2212 (CN), 3318-3196 (NH_2). MS, m/z: 339.97 (fig.9).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.70-8.00 (7H, m), 8.10 (2H, s).

Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate (219_{a-e}).

A mixture of cinnamonitrile derivatives (0.01 mol) and 5-chloro-8-quinolinol **(217)** (0.01 mol) was heated under reflux in absolute ethanol (50 ml) using a catalytic amount of piperidine for 6h. The solvent was evaporated under reduced pressure, cooled and the product was collected by filtration and recrystallized from methanol.

a: Brown crystal (65% yield), mp. 114 °C.
Analysis of $C_{21}H_{17}N_2O_3Cl$ (380.87). Calcd. %: C, 66.22; H, 4.50; N, 7.36; Cl, 9.32. Found %: C, 66.34; H, 4.46; N, 7.43; Cl, 9.26.
IR: 1731 (CO), 3472-3272 (NH_2) (fig.10). MS, m/z 380.97 (fig.11).
^{1}H-NMR ($CDCl_3$): 5.10 (1H, s), 1.30 (3H, t), 4.20 (2H, q), 7.10-8.50 (9H, m), 8.90 (2H, s).

b: Pale yellow crystals (79% yield), mp. 101 °C.
Analysis of $C_{22}H_{19}N_2O_4Cl$ (410.89). calcd. %: C, 64.30; H, 4.66; N, 6.82; Cl, 8.64. Found %: C, 64.44; H, 4.73; N, 6.73; Cl, 8.71.
IR: 1716 (CO), 3324-3180 (NH_2) (fig.12).

^{1}H-NMR ($CDCl_3$): 3.20 (3H, s), 1.35 (3H, t), 4.25 (2H, q), 5.10 (1H, s), 7.00-8.45 (8H, m), 8.90 (2H, s).

c: Pale brown crystals (72% yield), mp. 96 °C.
Analysis of $C_{21}H_{16}N_3O_5Cl$ (425.87). Calcd. %: C, 59.22; H, 3.79; N, 9.87; Cl, 8.34. Found %: C, 59.34; H, 3.73; N, 9.94; Cl, 8.28.
IR: 1700(CO), 3390-3242(NH_2) (fig.13).
^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 1.30 (3H,t), 4.15 (2H, q), 7.10-8.40 (8H, m).

d: Dark brown crystals (83% yield), mp. 119 °C.
Analysis of $C_{19}H_{15}N_2O_4Cl$ (370.83). Calcd. %: C, 61.54; H, 4.08; N, 7.56; Cl, 9.57. Found %: C, 61.65; H, 4.16; N, 7.47; Cl, 9.46.
IR: 1711 (CO), 3360-3186 (NH_2) (fig.14).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 1.35 (3H, t), 4.00 (2H, q), 6.80-7.90 (7H, m).

e: Orange crystals (80% yield), mp. 83 °C.
Analysis of $C_{19}H_{15}N_2O_3SCl$ (386.93). Calcd. %: C,58.98; H, 3.91; N, 7.24; S, 8.30; Cl, 9.18. Found %: C, 58.85; H, 3.83; N, 7.33; S, 8.22; Cl, 9.30.
IR: 1716 (CO), 3324-3196 (NH_2) (fig.15).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 1.35 (3H, t), 4.00 (2H, q), 6.60-7.80 (7H, m).

7-Aryl-5-chloro-10-methyl-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]-pyrano[3,2-h]quinolines (220_{a-e}).

General procedure: A solution of $\mathbf{218_{a-e}}$ (0.01 mol) in acetic anhydride/pyridine mixture (20 ml, 2:1 v/v) was heated under reflux on a steam bath for 8h and poured into ice cold water. The products were collected, washed several times with water and recrystallized from dioxane.

a: Dark brown crystals (76% yield), mp. 170 °C.
Analysis of $C_{21}H_{14}N_3O_2Cl$ (375.85). Calcd. %: C, 67.10; H, 3.76; N, 11.18; Cl, 9.45. Found %: C, 67.23; H, 3.82; N, 11.26; Cl, 9.53.

IR: 1655 (CO), 3390 (NH) (fig.16). MS, m/z: 375.85 (fig.16).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 3.40 (3H, s). 7.00-8.20 (9H, m).

b: Reddish brown crystals (78% yield), mp. 196 °C.

Analysis of $C_{22}H_{16}N_3O_3Cl$ (405.88). Calcd. %: C, 65.10; H, 3.97; N, 10.36; Cl, 8.75. Found %: C, 65.26; H, 3.91; N, 10.28; Cl, 8.69.

IR: 3432 (NH), 2930-2832 (CH aliph.) (fig.17).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 3.80 (3H, s), 3.40 (3H, s), 7.00-8.20 (8H, m).

c: Dark green crystals (80% yield), mp. 126 °C.

Analysis of $C_{21}H_{13}N_4O_4Cl$ (420.85). calcd. %: C, 59.93; H, 3.11; N, 13.32; Cl, 8.44. Found %: C, 59.80; H, 3.19; N, 13.41; Cl, 8.51.

IR: 1710 (CO), 3273 (NH) (fig.18).

^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.80 (3H, s), 7.00-8.20 (8H,m).

d: Pale brown crystals (88% yield), mp. 130 °C.

Analysis of $C_{19}H_{12}N_3O_3Cl$ (365.82). Calcd. %: C, 62.38; H, 3.31; N, 11.49; Cl, 9.70. Found %: C, 62.25; H, 2.35; N, 11.57; Cl, 9.62.

IR: 1696 (CO), 3421 (NH) (fig.19).

^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 6.70-8.15 (7H, m).

e: Dark brown crystals (85% yield), mp. 175 °C.

Analysis of $C_{19}H_{12}N_3O_2SCl$ (381.92). Calcd. %: C, 59.75; H, 3.17; N, 11.01; S, 8.41; Cl, 9.30. Found %: C,59.64; H, 3.12; N, 11.22; S, 8.47; Cl, 9.22.

IR: 1685 (CO), 3421 (NH) (fig.20).

^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 6.70-8.15 (7H, m).

8-Amino-7-aryl-5-chloro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (221_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol) and formamide (25 ml) was heated under reflux for 5h. The reaction mixture was allowed to cool and the product was collected and recrystallized from methanol.

a: Dark brown crystals (65% yield), mp. 110 °C.
Analysis of $C_{20}H_{13}N_4OCl$ (360.84). Calcd. %: C, 66.57; H, 3.63; N, 15.53; Cl, 9.84. Found %: C, 66.47; H, 3.70; N, 15.64; Cl, 9.78.
IR: 3440-3340 (NH_2), 3020 (CH arom.). MS, m/z: 360.83 (fig.21).
^{1}H-NMR (DMSO-d_6): 5.00 (1H, s), 8.25 (2H, s), 7.25-8.10 (10H, m) (fig.21).

b: Brown crystals (69% yield), mp. 109 °C.
Analysis of $C_{21}H_{15}N_4O_2Cl$ (390.87). Calcd. %: C, 64.53; H, 3.35; N, 14.34; Cl, 9.08. Found %: C, 64.44; H, 3.41; N, 14.42; Cl, 9.16.
IR: 3440-3340 (NH_2), 3020 (CH arom.).
^{1}H-NMR (DMSO-d_6): 3.60 (3H, s), 5.00 (1H, s), 7.25-8.10 (9H, m), 8.25 (2H, s).

c: Reddish brown crystals (71% yield) , mp. 135 °C.
Analysis of $C_{20}H_{12}N_5O_3Cl$ (405.85).Calcd. %: C, 59.18; H, 2.98; N, 17.26; Cl, 8.75. Found %: C, 59.03; H, 2.95; N, 17.33; Cl, 8.81.
IR: 3420-3310 (NH_2), 3020 (CH arom.). MS, m/z: 405.79.
^{1}H-NMR (CF_3COOD): 4.9 (1H, s), 7.25-8.40 (9H, m).

d: Brown crystals (78% yield), mp. > 300 °C.
Analysis of $C_{18}H_{11}N_4O_2Cl$ (350.81). Calcd. %: C, 61.62; H, 3.16; N, 15.97; Cl, 10.12. Found %: C, 61.73; H, 3.24; N, 15.88; Cl, 10.22.
IR: 3440-3340 (NH_2), 3020 (CH arom.).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.70-8.00 (8H, m).

e: Brown crystals (74% yield), mp. 116 °C.
Analysis of $C_{18}H_{11}N_4OSCl$ (366.91). Calcd. %: C, 58.92; H, 3.12; N, 15.27; S, 8.75; Cl, 9.68. Found %: C, 58.83; H, 3.08; N, 15.35; S, 8.61; Cl, 9.60.
IR: 3440-3340 (NH_2), 3030 (CH arom.).

7-Aryl-5-chloro-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]pyrano [3,2-h]quinolines (222_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol), formic acid (7 ml) in formamide (25 ml) was heated under reflux for 4h.The reaction mixture was allowed to cool. poured into ice cold water and the product was collected and recrystallized from dioxane.

a: Pale brown crystals (63% yield), mp. 115 °C.
Analysis of $C_{20}H_{12}N_3O_2Cl$ (361.83): Calcd. %: C, 66.39; H, 3.34; N, 11.62; Cl, 9.81. Found %: C, 66.50; H, 3.29; N, 11.54; Cl, 9.75.
IR: 3100 (NH), 1690 (CO). MS, m/z: 361.85 (fig.22).
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 7.15-8.20 (10H, m).

b: Reddish brown crystals (66% yield), mp. 88 °C.
Analysis of $C_{21}H_{14}N_3O_3Cl$ (391.85). Calcd. %: C, 64.36; H, 3.60; N, 10.73; Cl, 9.06. Found %: C, 64.23; H, 3.54; N, 10.67; Cl, 9.14.
IR: 3100 (NH), 1700 (CO). MS, m/z: 391.78
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.50 (3H, s), 7.15-8.20 (9H, m).

c: Pale green crystals (69% yield), mp. 105 °C.
Analysis of $C_{20}H_{11}N_4O_4Cl$ (406.83). Calcd. %: C, 59.04; H, 2.73; N, 13.78; Cl, 8.73. Found %: C, 59.16; H, 2.67; N, 13.84; Cl, 8.81.
IR: 3100 (NH), 1700 (CO). MS, m/z: 406.81.
^{1}H-NMR (CF_3COOD): 4.80 (1H, s),7.15-8.20 (9H,m).

d: Brown crystals (74% yield), mp. 235 °C.
Analysis of $C_{18}H_{10}N_3O_3Cl$ (351.79). Calcd. %: C, 61.45; H, 2.87; N, 11.95; Cl, 10.09. Found %: C, 61.56; H, 2.92; N, 11.89; Cl, 10.15.
IR: 3100 (NH), 1705 (CO), 3010 (CH arom.).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.60-7.80 (8H, m).

e: Yellowish brown crystals (68% yield). Calcd. %: C, 58.76; H, 2.74; N, 11.43; S, 8.73; Cl, 9.65. Found %: C, 58.67; H, 2.62; N, 11.51; S, 8.79; Cl, 9.73.

4-Aryl-6-chloro-3-cyano-2-(ethoxymethylenamino)-4H-pyrano [3,2-h]quinolines (223$_{a-e}$).

General procedure: A mixture of **218$_{a-e}$** (0.01 mol) and triethyl orthoformate (3 ml) in acetic anhydride (15 ml) was heated under reflux for 2h. The solid product was collected and recrystallized from methanol.

a: Pale brown crystals (71% yield), mp. 247 °C.
Analysis of $C_{22}H_{16}N_3O_2Cl$ (389.88). Calcd. %: C, 67.77; H, 4.14; N, 10.78; Cl, 9.11. Found %: C, 67.66; H, 4.22; N, 10.69; Cl, 9.21.
IR: 2208 (CN) (fig.23). MS, m/z: 389.88 (fig.24).
^{1}H-NMR ($CDCl_3$): 4.95 (1H, s), 1.65 (3H, t), 4.20 (2H, q), 7.20-8.30 (10H, m).

b: Brown crystals (61% yield), mp. 220 °C.
Analysis of $C_{23}H_{18}N_3O_3Cl$ (419.90). Calcd. %: C, 65.79; H, 4.32; N, 10.01; Cl, 8.45. Found %: C, 65.66; H, 4.29; N, 10.12; Cl, 8.51.
IR: 2208 (CN), 2930 (CH aliph.) (fig.25). MS, m/z: 420.
^{1}H-NMR ($CDCl_3$): 4.95 (1H, s), 1.60 (3H, t), 3.80 (3H, s), 4.10 (2H, q), 7.20-8.30 (9H, m).

c: Pale brown crystals (64% yield), mp. 129 °C.
Analysis of $C_{22}H_{15}N_4O_4Cl$ (434.88). Calcd. %: C, 60.76; H, 3.48; N, 12.89; Cl, 8.16. Found %: C, 60.85; H, 3.54; N, 12.97; Cl, 8.24.
IR: 2218 (CN), 2940 (CH aliph.) (fig.26). MS, m/z: 434.83.
^{1}H-NMR ($CDCl_3$): 4.95 (1H, s), 1.50 (3H, t), 4.30 (2H, q), 7.20-8.30 (9H, m), (fig.26).
^{13}C-NMR: 158.85, 150.87, 148.30, 133.42, 129.28, 123.98, 115.09, 77.30, 72.66, 69.90, 63.66, 61.47, 55.76, 53.84, 40.74, 30.69.

d: Dark brown crystals (77% yield), mp. > 300 °C.
Analysis of $C_{20}H_{14}N_3O_3Cl$ (379.84). Calcd. %: C, 63.24; H, 3.72; N, 11.07; Cl, 9.35. Found %: C, 63.14; H, 3.69; N, 11.14; Cl, 9.40.
IR: 2200 (CN), 2900 (CH aliph.), 3000 (CH arom.).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 1.60 (3H, t), 4.10 (2H, q), 6.60-7.80 (8H, m).

e: Dark brown crystals (73% yield), mp. 256 °C.

Analysis of $C_{20}H_{14}N_3O_2SCl$ (395.94). Calcd. %: C, 60.67; H, 3.56; N, 10.62; S, 8.11; Cl, 8.97. Found %: C, 60.56; H, 3.49; N, 10.73; S, 8.03; Cl, 8.86.

IR: 2218 (CN), 2919 (CH aliph.), 3078 (CH arom.) (fig.27).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 1.60 (3H, t), 4.10 (2H, q), 6.60-7.80 (8H, m).

7-Aryl-5-chloro-8-imino-9-phenyl-7H-pyrimido[4',5':6,5]pyrano-[3,2-h]quinolines (224_{a-e}).

General procedure: A mixture of **223_{a-e}** (0.01 mol) and aniline (0.01 mol) in absolute ethanol (50 ml) was refluxed for 3h. The precipitate was collected and recrystallized from ethanol.

a: Reddish brown crystals (58% yield), mp. 109 °C.
Analysis of $C_{26}H_{17}N_4OCl$ (436.94). Calcd. %: C, 71.47; H, 3.92; N, 12.83; Cl, 8.13. Found %: C, 71.57; H, 3.88; N, 12.91; Cl, 8.22.
IR: 3191 (NH) (fig.28). MS, m/z: 437.
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 7.10-8.20 (15H, m).

b: Pale yellow crystals (64% yield), mp. 251 °C.
Analysis of $C_{27}H_{19}N_4O_2Cl$ (466.96). Calcd. %: C, 69.44; H, 4.10; N, 12.00; Cl, 7.60. Found %: C, 69.32; H, 4.05; N, 12.10; Cl, 7.53.
IR: 3400 (NH), 2930 (CH aliph.) (fig.29). MS, m/z: 466.96 (fig.29).
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.40 (3H, s), 7.10-8.20 (14H, m).

c: Pale brown crystals (61% yield), mp. 244 °C.
Analysis of $C_{26}H_{16}N_5O_3Cl$ (481.94). Calcd. %: C, 64.79; H, 3.35; N, 14.54; Cl, 7.37. Found %: C, 64.88; H, 4.40; N, 14.60; Cl, 7.44.
IR: 3319 (NH), 2935 (CH aliph.) (fig.30). MS, m/z: 482.
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 7.10-8.25 (14H, m).
^{13}C-NMR: 158.44, 148.33, 133.42, 129.16, 122.64, 114.42, 76.98, 72.66, 70.38, 63.66, 61.47, 55.76, 53.84, 40.47, 30.89.

d: Reddish brown crystals (71% yield), mp. 127 °C.
Analysis of $C_{24}H_{15}N_4O_2Cl$ (426.90). Calcd. %: C, 67.52; H, 3.54; N, 13.13; Cl, 8.32. Found %: C, 67.41; H, 3.61; N, 13.24; Cl, 8.26.
IR: 3319 (NH), 3058 (CH arom.) (fig.31).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.60-7.80 (13H, m).

e: Pale brown crystals (66% yield), mp. 109 °C.

Analysis of $C_{24}H_{15}N_4OSCl$ (443). Calcd. %: C, 65.07; H, 3.41; N, 12.65; S, 7.25; Cl, 8.01. Found %: C, 65.19; H, 3.33, N, 12.54; S, 7.34; Cl, 8.12.

IR: 3334 (NH), 3026 (CH arom.) (fig.32). MS, m/z: 443.

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.60-7.80 (13H, m).

8-Amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano-[3,2-h]quinolines (225_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol) and ethyl cyanoacetate (0.01 mol) was fused for 2h. the solid product was collected and recrystallized from dioxane.

a: Brown crystals (60% yield), mp. 155 °C.

Analysis of $C_{22}H_{13}N_4O_2Cl$ (400.86). Calcd. %: C, 65.91; H, 3.27; N, 13.98; Cl, 8.86. Found %: C, 65.82; H, 3.32; N, 13.92; Cl, 8.93.

IR: 3334-3201 (NH_2), 2203 (CN) (fig.33). MS, m/z: 400.84.

^{1}H-NMR (CF_3COOD): 4.95 (1H, s), 7.00-8.10 (9H, m).

b: Pale brown crystals (61% yield), mp. 195 °C.

Analysis of $C_{23}H_{15}N_4O_3Cl$ (430.89). Calcd. %: C, 64.11; H, 3.51; N, 13.01; Cl, 8.24. Found %: C, 64.23; H, 3.46; N, 13.11; Cl, 8.31.

IR: 3329-3186 (NH_2), 2208 (CN) (fig.34).

^{1}H-NMR (CF_3COOD): 4.95 (1H, s), 3.80 (3H, s), 7.00-8.10 (8H, m) (fig.34).

c: Pale brown crystals (68% yield), mp. 130 °C.

Analysis of $C_{22}H_{12}N_5O_4Cl$ (445.87). Calcd. %: C, 59.26; H, 2.71; N, 15.71; Cl, 7.96. Found %: C, 59.15; H, 2.78; N, 15.60; Cl, 7.87.

IR: 3191-3104 (NH_2), 3319 (NH), 2192 (CN), 2976 (CH arom.) (fig.35).

^{1}H-NMR (CF_3COOD): 4.95 (1H, s), 7.00-8.10 (8H, m).

d: Brown crystals (72% yield), mp. 137 °C.

Analysis of $C_{20}H_{11}N_4O_3Cl$ (390.83). Calcd. %: C, 61.46; H, 2.84; N, 14.34; Cl, 9.08. Found %: C, 61.56; H, 2.80; N, 14.42; Cl, 9.17.

IR: 3319-3191 (NH_2), 2218 (CN) (fig.36).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.70-7.85 (7H, m).

e: Dark brown crystals (66% yield), mp. > 300 °C.

Analysis of $C_{20}H_{11}N_4O_2SCl$ (406.93). Calcd. %: C, 59.03; H, 2.73; N, 13.77; S, 7.89; Cl, 8.72. Found %: C, 59.13; H, 2.77; N, 13.84; S, 7.96; Cl, 8.67.

IR: 3191-3093 (NH_2), 3339 (NH), 2208 (CN) (fig.37).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.70-7.85 (7H, m).

5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines (226_{a-e}).

General procedure: To an ice cold solution of **218_{a-e}** (0.01 mol) in a mixture of acetic acid (20 ml) and hydrochloric acid (10 ml), sodium nitrite (0.01 mol in 10 ml water) was added with stirring for 30 minutes and the stirring was continued for 3h. The product was collected and recrystallized from diluted acetic acid.

a: Yellowish brown crystals (64% yield), mp. 170 °C.

Analysis of $C_{19}H_{10}N_4OCl_2$ (381.31). Calcd. %: C, 59.84; H, 2.64; N, 14.70; Cl, 18.62. Found %: C, 59.98; H, 2.71; N, 14.61; Cl, 18.51.

IR: 3000 (CH arom.).

^{1}H-NMR ($CDCl_3$): 4.90 (1H, s), 7.20-8.30 (9H, m).

b: Brown crystals (69% yield), mp. 114 °C.

Analysis of $C_{20}H_{12}N_4O_2Cl_2$ (411.34). Calcd. %: C, 58.40; H, 2.94; N, 13.62; Cl, 17.26. Found %: C, 58.26; H, 2.90; N, 13.50; Cl, 17.32.

IR: 2945 (CH arom.) (fig.38). MS, m/z: 411.

^{1}H-NMR ($CDCl_3$): 3.20 (3H, s), 4.90 (1H, s), 7.20-8.30 (8H, m).

c: Pale brown crystals (58% yield), mp. 187 °C.

Analysis of $C_{19}H_9N_5O_3Cl_2$ (426.31). Calcd. %: C, 53.53; H, 2.13; N, 16.43; Cl, 16.66. Found %: C, 53.62; H, 2.18; N, 16.54; Cl, 16.58.

IR: 3000 (CH arom.).

^{1}H-NMR ($CDCl_3$): 4.90 (1H, s), 7.20-8.30 (8H, m).

d: Dark brown crystals (55% yield), mp. 250 °C.

Analysis of $C_{17}H_8N_4O_2Cl_2$ (371.27). Calcd. %: C, 54.99; H, 2.17; N, 15.09; Cl, 19.12. Found %: C, 54.88; H, 2.22; N, 15.18; Cl, 19.05.

IR: 3083 (CH arom.) (fig.39).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.60-7.80 (7H, m).

e: Brown crystals (57% yield), mp. 200 °C.

Analysis of $C_{17}H_8N_4OSCl_2$ (387.3 7). Calcd. %: C, 52.71; H, 2.08; N, 14.47; S, 8.29; Cl, 18.33. Found %: C, 52.84; H, 2.15; N, 14.35; S, 8.38; Cl, 18.22.

IR: 3000 (CH arom.) (fig.40).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.60-7.80 (7H, m).

2-Amino-4-aryl-3-(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]-quinolines (227_{a-e}).

General procedure: A mixture of **218_{a-e}** (0.01 mol), ethylenediamine (0.011 mol) and p-toluensulfonic acid monohydrate (0.012 mol) was heated under reflux for 12h. The reaction mixture was made alkaline with a saturated aqueous solution of sodium carbonate and the precipitate was filtered off and recrystallized from proper solvent.

a: Yellow crystals from methanol (62% yield), mp. 180 °C.

Analysis of $C_{21}H_{17}N_4OCl$ (376.89). Calcd. %: C, 66.92; H, 4.55; N, 14.87; Cl, 9.42. Found %: C, 66.78; H, 4.48; N, 14.95; Cl, 9.35.

IR: 3288-3037 (NH_2), 3437 (NH) (fig.41). MS, m/z: 376.81.

^{1}H-NMR ($CDCl_3$): 4.95 (1H, s), 6.60 (2H, s), 8.95 (1H, s), 3.30 (2H, t), 3.90 (2H, t), 7.00-8.45 (9H, m) (fig.41).

b: Pale yellow crystals from dioxane (68% yield), mp. 161 °C.

Analysis of $C_{22}H_{19}N_4O_2Cl$ (406.91). Calcd. %: C, 64.93; H, 4.71; N, 13.77; Cl, 8.72. Found %: C, 64.85; H, 4.66; N, 13.85; Cl, 8.64.

IR: 3440-3340 (NH_2).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 3.35 (2H, t), 3.80 (2H, t), 3.30 (3H, s), 6.90-8.30 (8H, m).

c: Pale orange crystals from methanol (74% yield), mp. 148 °C.

Analysis of $C_{21}H_{16}N_5O_3Cl$ (421.89). Calcd. %: C, 59.78; H, 3.82; N, 16.60; Cl, 8.42. Found %: C, 59.87; H, 3.87; N, 16.54; Cl, 8.48.

IR: 3350-3211 (NH_2), 3452 (NH) (fig.42).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.40 (2H, t), 3.90 (2H, t), 6.70 (2H, s), 9.00 (1H, s), 7.00-8.40 (8H, m).

d: Brown crystals from ethanol (78% yield), mp. > 300 °C.
Analysis of $C_{19}H_{15}N_4O_2Cl$ (366.850. Calcd. %: C, 62.20; H, 4.12; N, 15.28; Cl, 9.68. Found %: C, 62.31; H, 3.95; N, 15.19; Cl, 9.79.
IR: 3360-3159 (NH_2), 3432 (NH) (fig.43).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 3.40 (2H, t), 3.80 (2H, t), 7.00-8.30 (7H, m).

e: Pale brown crystals from dioxane (71% yield) mp. 206 °C.
Analysis of $C_{19}H_{15}N_4OSCl$ (382.95). Calcd. %: C, 59.59; H, 3.95; N, 14.63; S, 8.38; Cl, 9.27. Found %: C, 59.47; H, 3.87; N, 14.71; S, 8.47; Cl, 9.36.
IR: 3216-3052 (NH_2), 3345 (NH) (fig.44).
^{1}H-NMR (CF_3COOD): 4.90 (1H, s), 3.40 (2H, t), 3.80 (2H, t). 7.00-8.40 (7H, m).

2,3,14-Trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines (228_{a-e}).

General procedure: To a suspension of **227_{a-e}** (0.01 mol) in triethyl orthoformate (0.018 mol), was added small amount of formic acid (0.5 ml) and the mixture was heated under reflux for 7h. After cooling to rt, the product was collected by filtration and recrystallized from diluted acetic acid.

a: Pale yellow crystals from dioxane (58% yield) mp. 295 °C.
Analysis of $C_{22}H_{15}N_4OCl$ (386.88). Calcd. %: C, 68.30; H, 3.91; N, 14.49; Cl, 9.18. Found %: C, 68.18; H, 3.85; N, 14.37; Cl, 9.25.
IR: 3058 (CH arom.) (fig.45). MS, m/z: 386.79.
^{1}H-NMR ($CDCl_3$): 4.95 (1H, s), 3.90-4.05 (4H, m), 7.10-8.50 (9H, m).

b: Yellow crystals from ethanol (65% yield), mp. 243 °C.
Analysis of $C_{23}H_{17}N_4O_2Cl$ (416.91). Calcd. %: C, 66.26; H, 4.11; N, 13.44; Cl, 8.52. Found %: C, 66.39; H, 4.18; N, 13.57; Cl, 8.46.
IR: 3058 (CH arom.), 2930-2832 (CH aliph.) (fig.46).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.40 (3H, s), 3.80-4.00 (4H, m), 7.00-8.40 (8H, m) (fig.46).

c: Pale brown crystals from ethanol (70% yield), mp. 257 °C.
Analysis of $C_{22}H_{14}N_5O_3Cl$ (431.88). Calcd. %: C, 61.18; H, 3.27; N, 16.22; Cl, 8.22. Found %: C, 61.31; H, 3.31; N, 16.36; Cl, 8.31.
IR: 3037 (CH arom.), 2925-2848 (CH aliph.) (fig.47).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.90-4.00 (4H, m), 7.00-8.35 (8H, m).

d: Brown crystals from ethanol (73% yield), mp. > 300 °C.
Analysis of $C_{20}H_{13}N_4O_2Cl$ (376.84). Calcd. %: C, 63.74; H, 3.48; N, 14.87; Cl, 9.42. Found %: C, 63.85; H, 3.57; N, 14.96; Cl, 9.55.
IR: 3052 (CH arom.), 2937 (CH aliph.).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.80-3.95 (4H, m), 6.85-8.10 (7H, m).

e: Brown crystals from methanol (67% yield), mp. 250 °C.
Analysis of $C_{20}H_{13}N_4OSCl$ (392.94). Calcd. %: C, 61.13; H, 3.34; N, 14.26; S, 8.17; Cl, 9.04. Found %: C, 61.28; H, 3.41; N, 14.11; S, 8.26; Cl, 9.18.
IR: 3042 (CH arom.), 2930 (CH aliph.) (fig.48).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 3.80-3.95 (4H, m) 6.80-8.00 (7H, m).

2,3,5,6,14-Pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines ($229_{a-e} - 232_{a-e}$).

General procedure: To a solution of **227_{a-e}** (0.01 mol) and the appropriate aldehyde (0.01 mol) or ketone (0.02 mol) in absolute ethanol (30 ml) was added concentrated hydrochloric acid (0.3 ml) and the mixture was stirred at 80-100 °C in a well stoppered round bottom flask fitted with reflux condenser for 12h. The product was isolated by column chromatography on silica gel with ethyl acetate/ methanol/ aq. Ammonia (6:2:2) as eluent.

229a: Dark brown crystals from methanol (35% yield), mp. > 300 °C.
Analysis of $C_{24}H_{19}N_4OCl$ (402.92). Calcd. %: C, 68.56; H, 4.75; N, 13.91; Cl, 8.81. Found %: C, 68.45; H, 4.66; N, 13.80; Cl, 8.72.
^{1}H-NMR ($CDCl_3$): 2.10 (3H, d), 3.50-3.90 (4H, m), 5.00 (1H, s), 2.8-3.0 (1H, q), 7.10-8.85 (9H, m) (fig.49).

b: Brown crystals from dioxane (31% yield), mp. 224 °C.

Analysis of $C_{24}H_{21}N_4O_2Cl$ (432.95). Calcd. %: C, 66.58; H, 4.89; N, 12.94; Cl, 8.20. Found %: C, 66.71; H, 4.78; N, 12.81; Cl, 8.31.

IR: 2960-2919 (CH aliph.), 3400 (NH) (fig.50).

^{1}H-NMR ($CDCl_3$): 2.00 (3H, d), 2.20 (3H, s), 3.50-3.90 (4H, m), 5.00 (1H, s), 5.45 (1H, m), 6.60 (1H, s), 7.10-8.80 (8H, m).

c: Brown crystals from ethanol (36% yield), mp. 242 °C.

Analysis of $C_{23}H_{18}N_5O_3Cl$ (447.92). Calcd. %: C, 61.67; H, 4.05; N, 15.64; Cl, 7.93. Found %: C, 61.53; H, 4.13; N, 15.51; Cl, 7.85.

^{1}H-NMR ($CDCl_3$): 2.00 (3H, d), 3.50-3.80 (4H, m), 5.00 (1H, s), 5.50 (1H, m), 6.60 (1H, s), 7.10-8.80 (8H, m).

d: Brown crystals from ethanol (39% yield), mp. > 300 °C.

Analysis of $C_{21}H_{17}N_4O_2Cl$ (392.89). Calcd. %: C, 64.19; H, 4.36; N, 14.26; Cl, 9.04. Found %: C, 64.31; H, 4.43; N, 14.14; Cl, 9.13.

^{1}H-NMR ($CDCl_3$): 2.00 (3H, d), 3.35 (3H, s), 3.50-3.90 (4H, m), 5.00 (1H, s), 5.40 (1H, m), 6.50 (1H, s), 6.80-8.50 (7H, m).

e: Brown crystals from dioxane (41% yield), mp. > 300 °C.

Analysis of $C_{21}H_{17}N_4OSCl$ (408.99). Calcd. %: C, 61.67; H, 4.19; N, 13.70; S, 7.85; Cl, 8.68. Found %: C, 61.53; H, 4.25; N, 13.84; S, 7.71; Cl, 8.57.

IR: 3400 (NH) (fig.51).

^{1}H-NMR ($CDCl_3$): 2.00 (3H, d), 3.50-3.80 (4H, m), 5.00 (1H, s), 5.50 (1H, m), 6.50 (1H, s), 6.70-8.60 (7H, m).

230a: Pale brown crystals from ethanol, mp. > 300 °C.

Analysis of $C_{24}H_{21}N_4OCl$ (416.95). Calcd. %: C, 69.13; H, 5.08; N, 13.44; Cl, 8.51. Found %: C, 69.29; H, 5.19; N, 13.56; Cl, 8.63.

IR: 3359 (NH), 3063 (CH arom.), 2966 (CH aliph.) (fig.52).

^{1}H-NMR ($CDCl_3$): 2.90 (6H, s), 3.40-3.70 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (9H, m) (fig.52).

b: Yellowish brown crystals from ethanol (34% yield), mp. > 300 °C.

Analysis of $C_{25}H_{23}N_4O_2Cl$ (446.97). Calcd. %: C, 67.18; H, 5.19; N, 12.54; Cl, 7.94. Found %: C, 67.32; H, 5.26; N, 12.41; Cl, 7.85.

IR: 3365 (NH), 3037 (CH arom.), 2930-2822 (CH aliph.) (fig.53).

^{1}H-NMR ($CDCl_3$): 3.20 (3H, s), 2.90 (6H, s), 3.40-3.80 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.00-8.60 (8H, m).

c: Brown crystals from ethanol (34% yield), mp. > 300 °C.

Analysis of $C_{24}H_{20}N_5O_3Cl$ (461.95). Calcd. %: C, 62.40; H, 4.36; N, 15.16; Cl, 7.69. Found %: C, 62.29; H, 4.47; N, 15.05; Cl, 7.58.

IR: 3380 (NH), 2996-2868 (CH aliph.) (fig.54).

^{1}H-NMR ($CDCl_3$): 2.90 (6H, s), 3.40-3.70 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (9H, m).

d: Greenish yellow crystals from dioxane (39% yield), mp. 290-292 °C.

Analysis of $C_{22}H_{19}N_4O_2Cl$ (406.91). Calcd. %: C, 64.93; H, 4.71; N, 13.77; Cl, 8.72. Found %: C, 64.78; H, 4.61; N, 13.63; Cl, 8.60.

IR: 3400 (NH), 2919 (CH aliph.) (fig.55).

^{1}H-NMR ($CDCl_3$): 2.80 (6H, s), 3.40-3.75 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

e: Dark brown crystals from ethanol (32% yield), mp. 248 °C.

Analysis of $C_{22}H_{19}N_4OSCl$ (423.01). Calcd. %: C, 62.46; H, 4.53; N, 13.25; S, 7.59; Cl, 8.39. Found %: C, 62.59; H, 4.42; N, 13.38; S, 7.46; Cl, 8.26.

IR: 3400 (NH) (fig.56). MS, m/z: 423.

^{1}H-NMR ($CDCl_3$): 2.80 (6H, s), 3.40-3.75 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.20 (7H, m).

231a: Pale brown crystals from methanol (58% yield), mp. 198 °C.

Analysis of $C_{26}H_{23}N_4OCl$ (442.98). Calcd. %: C, 70.49; H, 5.23; N, 12.65; Cl, 8.01. Found %: C, 70.38; H, 5.32; N, 12.76; Cl, 8.13.

IR: 3380 (NH), 2961-2863 (CH aliph.) (fig.57).

^{1}H-NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.70-4.05 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 7.10-8.70 (9H, m).

b: Pale brown crystals from methanol (55% yield), mp. > 300 °C.

Analysis of $C_{27}H_{25}N_4O_2Cl$ (473.01). Calcd. %: C, 68.56; H, 5.33; N, 11.85; Cl, 7.51. Found %: C, 68.42; H, 5.41; N, 11.73; Cl, 7.69.

IR: 3365 (NH), 2945 (CH aliph.) (fig.58). MS, m/z: 473.

^{1}H-NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.55 (3H, s), 3.70-4.50 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 7.00-8.60 (8H, m).

c: Brown crystals from ethanol (60% yield), mp. 250 °C.

Analysis of $C_{26}H_{22}N_5O_3Cl$ (487.99). Calcd. %: C, 63.99; H, 4.54; N, 14.36; Cl, 7.28. Found %: C, 63.84; H, 4.61; N, 14.45; Cl, 7.39.

IR: 3467 (NH), 3053 (CH arom.), 2925 (CH aliph.) (fig.59). MS, m/z: 488.

^{1}H-NMR ($CDCl_3$): 1.50-1.90 (8H, m), 3.80-4.10 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.10-8.70 (8H, m) (fig.59).

d: Dark brown crystals from dioxane (56% yield), mp. > 300 °C.

Analysis of $C_{24}H_{21}N_4O_2Cl$ (432.95). Calcd. %: C, 66.58; H, 4.89; N, 12.94; Cl, 8.20. Found %: C, 66.42; H, 4.97; N, 12.79; Cl, 8.36.

IR: 3396 (NH), 2950 (CH aliph.) (fig.60).

^{1}H-NMR ($CDCl_3$): 1.40-1.80 (8H, m), 3.70-4.00 (4H, m), 5.00 (1H, s), 6.50 (1H, s), 6.80-8.40 (7H, m).

e: Brown crystals from dioxane (59% yield), mp. > 300 °C.

Analysis of $C_{24}H_{21}N_4OSCl$ (449.05). Calcd. %: C, 64.19; H, 4.71; N, 12.48; S, 7.15; Cl, 7.91. Found %: C, 64.36; H, 4.64; N, 12.33; S, 7.27; Cl, 7.82.

IR: 3406 (NH) 2945 (CH aliph.)(fig.61). MS, m/z: 449.

232a: Yellowish green crystals from methanol (56% yield), mp. > 300 °C.

Analysis of $C_{27}H_{25}N_4OCl$ (457.01). Calcd. %: C, 70.96; H, 5.51; N, 12.26; Cl, 7.77. Found %: C, 70.82; H, 5.43; N, 12.17; Cl, 7.84.

IR: 3421 (NH), 2935 (CH aliph.) (fig.62). MS, m/z: 457.

b: Yellow crystals from dioxane (59% yield), mp. > 300 °C.

Analysis of $C_{28}H_{27}N_4O_2Cl$ (487.04). Calcd. %: C, 69.05; H, 5.59; N, 11.51; Cl, 7.29. Found %: C, 69.18; H, 5.65; N, 11.38; Cl, 7.18.

IR: 3375 (NH), 2940 (CH aliph.) (fig.63).

^{1}H-NMR ($CDCl_3$): 1.40-1.80 (10H, m), 3.65 (3H, s), 3.90-4.10 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 7.10-8.50 (8H, m).

c: Pale brown crystals from methanol (60% yield), mp. 178 °C.
Analysis of $C_{27}H_{24}N_5O_3Cl$ (502.01). Calcd. %: C, 64.59; H, 4.82; N, 13.95; Cl, 7.07. Found %: C, 64.43; H, 4.74; N, 13.80; Cl, 7.19.
IR: 3339 (NH), 2930-2858 (CH aliph.) (fig.64).
^{1}H-NMR ($CDCl_3$): 1.50-1.90 (10H, m), 3.90-4.10 (4H, m), 5.00 (1H, s), 6.70 (1H, s), 7.10-8.60 (8H, m).

d: Brown crystals from dioxane (63% yield), mp. > 300 °C.
Analysis of $C_{25}H_{23}N_4O_2Cl$ (446.97). Calcd. %: C, 67.18; H, 5.19; N, 12.54; Cl, 7.94. Found %: C, 67.30; H, 5.28; N, 12.41; Cl, 7.82.
IR: 3391 (NH), 2930 (CH aliph.) (fig.65).

e: Dark brown crystals from dioxane (61% yield), mp. > 300 °C.
Analysis of $C_{25}H_{23}N_4OSCl$ (463.07). Calcd. %: C, 64.84; H, 5.01; N, 12.10; S, 6.93; Cl, 7.67. Found %: C, 64.69; H, 5.12; N, 12.25; S, 6.81; Cl, 7.78.
IR: 3380 (NH) 2930 (CH aliph.)(fig.66).
^{1}H-NMR ($CDCl_3$): 1.50-1.80 (7H, m), 3.80-4.00 (4H, m), 5.00 (1H, s), 6.60 (1H, s), 6.80-8.40 (7H, m).

5-Thioxo-2,3,6,14-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano-[3,2h]quinolines (233_{a-e}).

General procedure: A mixture of **227_{a-e}** (0.01 mol), carbon disulfide (5 ml) in ethanol (50 ml) and two pellets of potassium hydroxide (0.17 g, 0.003 mol) was heated under reflux on water bath for 6h. the solid product obtained was dissolved in water and then acidified with acetic acid and recrystallized from diluted acetic acid.

a: Yellow crystals (63% yield), mp. > 300 °C.
Analysis of $C_{22}H_{15}N_4OSCl$ (418.98). Calcd. %: C, 63.06; H, 3.61; N, 13.38; S, 7.66; Cl, 8.47. Found %: C, 63.17; H, 3.50; N, 13.25; S, 7.52; Cl, 8.35.
IR: 3432 (NH), 3058 (CH arom.) (fig.67).
^{1}H-NMR (CF_3COOD): 3.70-3.90 (4H, m), 4.90 (1H, s), 7.00-8.50 (9H, m).

b: Yellowish green crystals (61% yield), mp. 202 °C.

Analysis of $C_{23}H_{17}N_4O_2SCl$ (449.01). Calcd. %: C, 61.52; H, 3.82; N, 12.48; S, 7.15; Cl, 7.91. Found %: C, 61.64; H, 3.74; N, 12.33; S, 7.29; Cl, 7.75.
IR: 3375 (NH), 3058 (CH arom.), 2930-2822 (CH aliph.) (fig.68).
MS, m/z: 449.

c: Pale brown crystals (70% yield), mp. 122 °C.
Analysis of $C_{22}H_{14}N_5O_3SCl$ (463.98). Calcd. %: C, 56.95; H, 3.04; N, 15.10; S, 6.92; Cl, 7.65. Found %: C, 56.81; H, 3.15; N, 15.21; S, 6.79; Cl, 7.53.
IR: 3350 (NH), 3063 (CH arom.), 2920 (CH aliph.) (fig.69).
^{1}H-NMR (CF_3COOD): 3.80-4.00 (4H, m), 5.00 (1H, s), 7.10-8.60 (8H, m).

d: Dark brown crystals (70% yield), mp. 122 °C.
Analysis of $C_{20}H_{13}N_4O_2SCl$ (408.94). Calcd. %: C, 58.74; H, 3.20; N, 13.70; S, 7.85; Cl, 8.68. Found %: C, 56.58; H, 3.12; N, 13.83; S, 7.71; Cl, 8.53.
IR: 3391 (NH), 3053 (CH arom.), 2919 (CH aliph.) (fig.70).
^{1}H-NMR (CF_3COOD): 3.70-3.95 (4H, m), 5.00 (1H, s), 6.80-8.40 (7H, m).

e: Dark brown crystals (64% yield), mp. 225 °C.
Analysis of $C_{20}H_{13}N_4OS_2Cl$ (425.04). Calcd. %: C, 56.51; H, 3.08; N, 13.19; S, 7.55; Cl, 8.35. Found %: C, 56.66; H, 3.19; N, 13.05; S, 7.42; Cl, 8.23.
IR: 3400 (NH), 3053 (CH arom.) (fig.71).

5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines (234_{a-e}).

General procedure: A mixture of **226_{a-e}** (0.002 mol) and hydrazine hydrate (2 ml, 98%) in ethanol (30 ml) was heated under reflux for 6h. The product obtained after cooling was filtered off, washed with water and recrystallized from ethanol.

a: Yellow crystals (80% yield), mp. 199 °C.
Analysis of $C_{19}H_{13}N_6OCl$ (376.85). Calcd. %: C, 60.55; H, 3.48; N, 22.31; Cl, 9.42. Found %: C, 60.69; H, 3.57; N, 22.45; Cl, 9.56.
IR: 3324-3180 (NH_2), 3473 (NH), 3048 (CH arom.), 2935-2893 (CH aliph.) (fig.72).
^{1}H-NMR ($CDCl_3$): 4.30 (2H, s), 5.00 (1H, s), 7.00-8.60 (9H, m) (fig.72).

b: Pale brown crystals (77% yield), mp. 195 °C.

Analysis of $C_{20}H_{15}N_6O_2Cl$ (406.88). Calcd. %: C, 59.04; H, 3.72; N, 20.66; Cl, 8.73. Found %: C, 59.17; H, 3.81; N, 20.54; Cl, 8.60.

IR: 3350-3201 (NH_2) (fig.73).

c: Brown crystals (66% yield), mp. 148 °C.

Analysis of $C_{19}H_{12}N_7O_3Cl$ (421.86). Calcd. %: C, 54.09; H, 2.87; N, 23.25; Cl, 8.42. Found %: C, 54.24; H, 2.94; N, 23.37; Cl, 8.51.

IR: 3339-3206 (NH_2) (fig.74).

^{1}H-NMR ($CDCl_3$): 4.40 (2H, s), 5.00 (1H, s), 7.10-8.60 (8H, m), 8.95 (1H, s).

d: Brown crystals (75% yield), mp. 147 °C.

Analysis of $C_{17}H_{11}N_6O_2Cl$ (366.82). Calcd. %: C, 55.66; H, 3.02; N, 22.92; Cl, 9.68. Found %: C, 55.54; H, 2.94; N, 22.79; Cl, 9.56.

IR: 3324-3201 (NH_2) (fig.75).

e: Brown crystals (68% yield), mp. 260 °C.

Analysis of $C_{17}H_{11}N_6OSCl$ (397.84). Calcd. %: C, 51.32; H, 2.79; N, 21.13; S, 8.07; Cl, 8.92. Found %: C, 51.47; H, 2.88; N, 21.28; S, 8.16; Cl, 8.79.

^{1}H-NMR ($CDCl_3$): 4.30 (2H, s), 5.00 (1H, s), 6.75-8.40 (7H, m), 8.80 (1H, s).

14-Aryl-12-chloro[1,2,4]triazolo[3",4"-f][1,2,3]triazino[4',5':6,5]pyrano-[3,2-h]quinolines (235_{a-e}).

General procedure: A mixture of **234_{a-e}** (0.001 mol) in formic acid (20 ml) was heated under reflux for 8h. The reaction mixture was concentrated in vacuo and the solid product was collected, washed with water and recrystallized from methanol.

a: Brown crystals (74% yield), mp. 178 °C.

Analysis of $C_{20}H_{11}N_6OCl$ (386.85). Calcd. %: C, 62.09; H, 2.87; N, 21.73; Cl, 9.18. Found %: C, 62.21; H, 2.94; N, 21.62; Cl, 9.25.

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.60 (1H, s), 7.10-8.60 (9H, m) (fig.76).

b: Brown crystals (68% yield), mp. 252 °C.

Analysis of $C_{21}H_{13}N_6O_2Cl$ (416.87). Calcd. %: C, 60.50; H, 3.14; N, 20.17; Cl, 8.52. Found %: C, 60.35; H, 3.08; N, 20.29; Cl, 8.44.

^{1}H-NMR ($CDCl_3$): 3.65 (3H, s), 5.00 (1H, s), 6.60 (1H, s), 7.00-8.40 (8H, m).

c: Dark brown crystals (61% yield), mp. > 300 °C.
Analysis of $C_{20}H_{10}N_7O_3Cl$ (431.85). Calcd. %: C, 55.62; H, 2.33; N, 22.71; Cl, 8.22. Found %: C, 55.49; H, 2.40; N, 22.60; Cl, 8.35.
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.60 (1H, s), 7.10-8.50 (8H, m).

d: Dark brown crystals (67% yield), mp. > 300 °C.
Analysis of $C_{18}H_9N_6O_2Cl$ (376.81). Calcd. %: C, 57.37; H, 2.41; N, 22.31; Cl, 9.42. Found %: C, 57.48; H, 2.52; N, 22.20; Cl, 9.31.
^{1}H-NMR ($CDCl_3$): 4.90 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

e: Dark brown crystals (59% yield), mp. > 300 °C.
Analysis of $C_{18}H_9N_6OSCl$ (392.91). Calcd. %: C, 55.02; H, 2.31; N, 21.39; S,8.17; Cl, 9.04. Found %: C, 55.15; H, 2.24; N, 21.26; S, 8.20; Cl, 9.17.
^{1}H-NMR ($CDCl_3$): 4.90 (1H, s), 6.50 (1H, s), 6.80-8.30 (7H, m).

14-Aryl-12-chloro-3-thioxo[1,2,4]triazolo[3",4"-f][1,2,3]triazino-[4',5':6,5]pyrano[3,2-h]quinolines (236_{a-e}).

General procedure: A mixture of **234_{a-e}** (0.01 mol), carbon disulfide (5 ml) in ethanol (50 ml) and two pellets of potassium hydroxide was heated under reflux for 6h. The solid product obtained was dissolved in water and then acidified with acetic acid and recrystallized from diluted acetic acid.

a: Pale brown crystals (64% yield), mp. 168 °C.
Analysis of $C_{20}H_{11}N_6OSCl$ (418.95). Calcd. %: C, 57.33; H, 2.65; N, 20.07; S, 7.66; Cl, 8.47. Found %: C, 57.48; H, 2.74; N, 20.19; S, 7.52; Cl, 8.34.
IR: 3334 (NH), 1190 (CS) (fig.80).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.80-8.10 (9H, m), 8.50 (1H, s).

b: Pale brown crystals (58% yield), mp. 195 °C.
Analysis of $C_{21}H_{13}N_6O_2SCl$ (448.97). Calcd. %: C, 56.18; H, 2.92; N, 18.72; S, 7.15; Cl, 7.91. Found %: C, 56.06; H, 2.84; N, 18.62; S, 7.26; Cl, 7.82.
IR: 3324 (NH) (fig.81).
^{1}H-NMR (CF_3COOD): 3.50 (3H, s), 5.00 (1H, s), 7.10-8.40 (8H, m).

c: Reddish brown crystals (56% yield), mp. 101 °C.

Analysis of $C_{20}H_{10}N_7O_3SCl$ (463.95). Calcd. %: C, 51.77; H, 2.17; N, 21.14; S, 6.92; Cl, 7.52. Found %: C, 51.63; H, 2.25; N, 21.28; S, 6.81; Cl, 7.52.

IR: 3350 (NH) (fig.82).

d: Dark brown crystals (60% yield), mp. > 300 °C.

Analysis of $C_{18}H_9N_6O_2SCl$ (408.91). Calcd. %: C, 52.87; H, 2.22; N, 20.56; S, 7.85; Cl, 8.68. Found %: C, 52.71; H, 2.31; N, 20.41; S, 7.70; Cl, 8.52.

IR: 3206 (NH) (fig.83).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.80-8.30 (7H, m).

e: Brown crystals (54% yield), mp. 182 °C.

Analysis of $C_{18}H_9N_6OS_2Cl$ (425.01). Calcd. %: C, 50.87; H, 2.14; N, 19.78; S, 15.11; Cl, 8.35. Found %: C, 50.92; H, 2.21; N, 19.66; S, 15.23; Cl, 8.23.

IR: 3355 (NH) (fig.84). MS, m/z: 425.

5-Aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines (237_{a-e}).

General procedure: To a well-stirred solution of **234_{a-e}** (0.002 mol) in glacial acetic acid (50 ml), a solution of sodium nitrite (1 g in 10 ml of water) was added at rt and stirring was continued for 1h. The solid obtained was filtered off, washed with water and recrystallized from acetic acid.

a: Brown crystals (61% yield), mp. 163 °C.

Analysis of $C_{19}H_{10}N_7OCl$ (387.84). Calcd. %: C, 58.84; H, 2.60; N, 25.29; Cl, 9.15. Found %: C, 58.71; H, 2.50; N, 25.15; Cl, 9.26.

IR: 2182 (N_3) (fig.85).

b: Brown crystals (59% yield), mp. 185 °C.

Analysis of $C_{20}H_{12}N_7O_2Cl$ (417.87). Calcd. %: C, 57.48; H, 2.90; N, 23.47; Cl, 8.50. Found %: C, 57.33; H, 2.83; N, 23.32; Cl, 8.41.

IR: 2121 (N_3) (fig.86).

^{1}H-NMR ($CDCl_3$): 3.40 (3H, s), 5.00 (1H, s), 7.00-8.30 (8H, m) (fig.86).

c: Brown crystals (55% yield), mp. 135 °C.

Analysis of $C_{19}H_9N_7O_3Cl$ (432.84). Calcd. %: C, 52.72; H, 2.10; N, 25.89; Cl, 8.20. Found %: C, 52.85; H, 2.17; N, 25.77; Cl, 8.07.

IR: 2182 (N_3) (fig.87).

d: Dark brown crystals (63% yield), mp. > 300 °C.

Analysis of $C_{17}H_8N_7O_2Cl$ (377.80). Calcd. %: C, 54.04; H, 2.14; N, 25.96; Cl, 9.40. Found %: C, 54.19; H, 2.05; N, 25.80; Cl, 9.27.

IR: 2126 (N_3) (fig.88).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.80-8.20 (7H, m).

e: Brown crystals (57% yield), mp. > 300 °C.

Analysis of $C_{17}H_8N_7OSCl$ (393.90). Calcd. %: C, 51.83; H, 2.05; N, 24.90; S, 8.15; Cl, 9.01. Found %: C, 51.66; H, 2.16; N, 24.74; S, 8.29; Cl, 9.16.

IR: 2126 (N_3) (fig.89).

^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.80-8.20 (7H, m).

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylates (238_{a-e}).

General procedure: A mixture of **219_{a-e}** (0.01 mol) and 2,5-dimethoxytetrahydrofuran (0.01 mol) in acetic acid (50 ml) was heated under reflux for 2h. After cooling, the precipitate formed was filtered off and recrystallized from ethanol.

a: Pale brown crystals (62% yield), mp. 126 °C.

Analysis of $C_{25}H_{19}N_2O_3Cl$ (430.92). Calcd. %: C, 69.68; H, 4.44; N, 6.50; Cl, 8.24. Found %: C, 69.82; H, 4.48; N, 6.41; Cl, 8.16.

IR: 1716 (CO) (fig.90). MS, m/z: 431 (fig.91).

^{1}H-NMR ($CDCl_3$): 1.38 (3H, t), 4.30 (2H, q), 5.10 (1H, s), 6.40 (2H, m), 6.75 (2H, m), 7.10-8.60 (9H, m).

b: Brown crystals (71% yield), mp. 89 °C.

Analysis of $C_{26}H_{21}N_2O_4Cl$ (460.95). Calcd. %: C, 67.74; H, 4.59; N, 6.08; Cl, 7.70. Found %: C, 67.61; H, 4.51; N, 6.16; Cl, 7.83.

IR: 1701(CO) (fig.92).

^{1}H-NMR ($CDCl_3$): 3.30 (3H, s), 1.35 (3H, t), 4.30 (2H, q), 5.00 (1H, s), 6.50 (2H, m), 6.80 (2H, m), 7.20-8.50 (8H, m) (fig.92).

c: Pale brown crystals (65% yield), mp. 142 °C.

Analysis of $C_{25}H_{18}N_3O_5Cl$ (475.92). Calcd. %: C, 63.09; H, 3.81; N, 8.83; Cl, 7. 46. Found %: C, 63.20; H, 3.76; N, 8.78; Cl, 7.35.

IR: 1710 (CO) (fig.93).

d: Brown crystals (74% yield), mp. 176 °C.

Analysis of $C_{23}H_{17}N_2O_4Cl$ (420.89). Calcd. %: C, 65.63; H, 4.07; N, 6.66; Cl, 8.44. Found %: C, 65.74; H, 4.12; N, 6.74; Cl, 8.35.

IR: 1721(CO) (fig.94).

^{1}H-NMR ($CDCl_3$): 1.40 (3H, t), 4.30 (2H, q), 5.10 (1H, s), 6.40 (2H, m), 6.60 (2H, m), 6.80-8.20 (7H, m).

e: Brown crystals (68% yield), mp. 98 °C.

Analysis of $C_{23}H_{17}N_2O_3SCl$ (436.99). Calcd. %: C, 63.21; H, 3.92; N, 6.41; S, 7.35; Cl, 8.12. Found %: C, 63.33; H, 3.84; N, 6.31; S, 7.42; Cl, 8.21.

IR: 1721(CO) (fig.95).

2-(1-pyrrolyl)-4aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbohydrazide (239_{a-e}).

General procedure: To a solution of the ester **238_{a-e}** (0.01 mol) in hot ethanol (60 ml) was added an excess of hydrazine hydrate (5 ml, 98%) and the reaction mixture was refluxed for 5h. The solide product obtained was filtered off and recrystallized from diluted acetic acid.

a: Yellowish brown crystals (65% yield), mp. 134 °C.

Analysis of $C_{23}H_{17}N_4O_2Cl$ (416.91). Calcd. %: C, 66.26; H, 4.11; N, 13.44; Cl, 8.52. Found %: C, 66.15; H, 4.16; N, 13.50; Cl, 8.61.

IR: 1700 (CO), 3324-3206 (NH_2), 3452 (NH) (fig.96). MS, m/z: 417 (fig.97).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.40 (2H, m), 6.70 (2H, m), 7.10-8.60 (9H, m) (fig.97).

b: Pale brown crystals (75% yield), mp. 151 °C.

Analysis of $C_{24}H_{19}N_4O_3Cl$ (446.93). Calcd. %: C, 64.49; H, 4.29; N, 12.54; Cl, 7.94. Found %: C, 64.58; H, 4.34; N, 12.47; Cl, 7.85.

IR: 1716 (CO), 3312-3202 (NH_2), 3450 (NH).

^{1}H-NMR (CF_3COOD): 3.40 (3H, s), 5.10 (1H, s), 6.40 (2H, m), 6.70 (2H, m), 7.10-8.40 (8H, m).

c: Yellowish brown crystals (69% yield), mp. 121 °C.
Analysis of $C_{23}H_{16}N_5O_4Cl$ (461.91). Calcd. %: C, 59.80; H, 3.49; N, 15.17; Cl, 7.69. Found %: C, 59.95; H, 3.42; N, 15.23; Cl, 7.54.
IR: 1710 (CO), 3300-3200 (NH_2), 3450 (NH).

d: Pale brown crystals (78% yield), mp. 159 °C.
Analysis of $C_{21}H_{15}N_4O_3Cl$ (406.87). Calcd. %: C, 61.99; H, 3.72; N, 13.77; Cl, 8.37. Found %: C, 61.86; H, 3.67; N, 13.69; Cl, 8.50.
IR: 1700 (CO), 3320-3215 (NH_2), 3435 (NH).
^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.20 (2H, m), 6.60 (2H, m), 6.80-8.50 (7H, m).

e: Pale brown crystals (72% yield), mp. > 340 °C.
Analysis of $C_{21}H_{15}N_4O_2SCl$ (422.97). Calcd. %: C, 59.63; H, 3.58; N, 13.25; S, 7.59; Cl, 8.39. Found %: C, 59.79; H, 3.62; N, 13.19; S,7.68; Cl, 8.24.
IR: 1700 (CO), 3310-3200 (NH_2), 3420 (NH).

2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines (240_{a-e}).

General procedure: A mixture of **239_{a-e}** (0.01 mol) and excess of acetylacetone (10 ml) was refluxed for 5h. The excess acetylacetone was eliminated in vacuo and the solid product was collected and recrystallized from ethanol.

a: Brown crystals (61% yield), mp. 231 °C.
Analysis of $C_{28}H_{21}N_4O_2Cl$ (481). Calcd. %: C, 69.91; H, 4.40; N, 11.65; Cl, 7.38. Found %: C, 69.79; H, 4.37; N, 11.72; Cl, 7.46.
IR: 1701(CO) (fig.98). MS, m/z: 481.44 (fig.99).
^{1}H-NMR ($CDCl_3$): 1.80 (6H, s), 5.00 (1H, s), 6.30 (2H, m), 6.55 (2H, m), 7.10-8.50 (9H, m) (fig.99).

b: Yellowish brown crystals (70% yield), mp. 173 °C.
Analysis of $C_{29}H_{23}N_4O_2Cl$ (495.01). Calcd. %: C, 70.36; H, 4.68; N, 11.32; Cl, 7.17. Found %: C, 70.47; H, 4.74; N, 11.41; Cl, 7.28.

IR: 1706 (CO) (fig.100).

^{1}H-NMR ($CDCl_3$): 3.30 (3H, s), 5.10 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.20-8.50 (8H, m).

c: Pale brown crystals (65% yield), mp. 133 °C.
Analysis of $C_{28}H_{20}N_5O_4Cl$ (526). Calcd. %: C, 63.93; H, 3.83; N, 13.32; Cl, 6.75. Found %: C, 63.83; H, 3.77; N, 13.24; Cl, 6.65.
IR: 1720 (CO).

d: Yellowish brown crystals (74% yield), mp. > 340 °C.
Analysis of $C_{26}H_{19}N_4O_3Cl$ (470.95). Calcd. %: C, 66.30; H, 4.07; N, 11.90; Cl, 7.54. Found %: C, 66.42; H, 4.13; N, 11.81; Cl, 7.42.
IR: 1716 (CO).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.10-8.20 (7H, m).

e: Brown crystals (68% yield), mp. 112 °C.
Analysis of $C_{26}H_{19}N_4O_2SCl$ (487.05). Calcd. %: C, 64.11; H, 3.93; N, 11.51; S, 6.59; Cl, 7.29. Found %: C, 64.22; H, 3.87; N, 11.43; S, 6.66; Cl, 7.18.
IR: 1722 (CO).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 7.20-8.40 (7H, m).

2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-oylazid (241_{a-e}).

General procedure: To a solution of **239_{a-e}** (0.01 mol) in glacial acetic acid (40 ml), a solution of sodium nitrite (0.01 mol in 10 ml water) was added at rt with stirring. Stirring was continued for 30 minutes and the precipitate was filtered off, washed with water and recrystallized from benzene.

a: Pale brown crystals (62% yield), mp. 185 °C.
Analysis of $C_{23}H_{14}N_5O_2Cl$ (427.89). Calcd. %: C, 64.56; H, 3.30; N, 16.37; Cl, 8.30. Found %: C, 64.68; H, 3.38; N, 16.48; Cl, 8.19.
IR: 2213 (N_3), 1716 (CO) (fig.101). MS, m/z: 427.71 (fig.101).

b: Pale brown crystals (67% yield), mp. 108 °C.

Analysis of $C_{24}H_{16}N_5O_3Cl$ (457.92). Calcd. %: C, 62.95; H, 3.52; N, 15.30; Cl, 7.75. Found %: C, 62.82; H, 3.47; N, 15.43; Cl, 7.82.

IR: 2212 (N_3), 1705 (CO) (fig.102).

^{1}H-NMR ($CDCl_3$): 3.50 (3H, s), 5.10 (1H, s), 6.40 (2H, m), 6.60 (2H, m), 7.30-8.50 (8H, m) (fig.102).

c: Pale brown crystals (61% yield), mp. 194 °C.
Analysis of $C_{23}H_{13}N_5O_4Cl$ (458.88). Calcd. %: C, 60.20; H, 2.86; N, 15.27; Cl, 7.74. Found %: C, 60.31; H, 2.94; N, 15.49; Cl, 7.81.
IR: 2210 (N_3), 1700 (CO).

d: Dark brown crystals (70% yield), mp. 338 °C.
Analysis of $C_{21}H_{12}N_5O_3Cl$ (417.86). Calcd. %: C, 60.36; H, 2.90; N, 16.76; Cl, 8.50. Found %: C, 60.48; H, 2.84; N, 16.88; Cl, 8.43.
IR: 2078 (N_3), 1706 (CO) (fig.103).
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.30 (2H, m), 6.50 (2H, m), 6.80-8.10 (7H, m).

e: Dark brown crystals (74% yield), mp. 257 °C.
Analysis of $C_{21}H_{12}N_5O_2SCl$ (433.96). Calcd. %: C, 58.12; H, 2.79; N, 16.14; S,7.40; Cl, 8.18. Found %: C, 58.22; H, 2.87; N, 16.25; S, 7.51; Cl, 8.25.
IR: 2356 (N_3), 1680 (CO) (fig.104).

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbamate (242_{a-e}).

General procedure: Each compound of **241_{a-e}** (0.01 mol) was heated under reflux in excess of absolute ethanol (50 ml) for 2h. The reaction mixture was concentrated and left to cool . The solid product was recrystallized from ethanol.

a: Brown crystals (72% yield), mp. > 340 °C.
Analysis of $C_{25}H_{20}N_3O_3Cl$ (445.94). Calcd. %: C, 67.33; H, 4.52; N, 9.43; Cl, 7.96. Found %: C, 67.47; H, 4.58; N, 9.36; Cl, 8.04.
IR: 1707 (CO), 3375 (NH), (fig.105). MS, m/z: 446.02 (fig.106).
^{1}H-NMR (CF_3COOD): 2.10 (3H, t), 4.20 (2H, q), 5.10 (1H, s), 6.30 (2H, m), 6.60 (2H, m), 7.30-8.50 (9H, m) (fig.106).

b: Dark brown crystals (76% yield), mp. 192 °C.

Analysis of $C_{26}H_{22}N_3O_4Cl$ (475.97). Calcd. %: C, 65.61; H, 4.66; N, 8.83; Cl,7.46. Found %: C, 65.45; H, 5.58; N, 8.92; Cl, 7.62.

IR: 1706 (CO), 3457 (NH) (fig.107).

c: Brown crystals (70% yield), mp. > 340 °C.

Analysis of $C_{25}H_{19}N_4O_5Cl$ (490.94). Calcd. %: C, 61.16; H, 3.90; N, 11.42; Cl, 7.23. Found %: C, 61.30; H, 3.78; N, 11.28; Cl, 7.34.

IR: 1700 (CO), 3421 (NH) (fig.108).

^{1}H-NMR (CF_3COOD): 2.10 (3H, q), 4.10 (2H, q), 5.10 (1H, s), 6.30 (2H, m), 6.60 (2H, m), 7.20-8.50 (8H, m).

d: Dark brown crystals (79% yield), mp. > 340 °C.

Analysis of $C_{23}H_{18}N_3O_4Cl$ (435.90). Calcd. %: C, 63.37; H, 4.16; N, 9.64; Cl, 8.14. Found %: C, 63.22; H, 4.24; N, 9.75; Cl, 8.29.

IR: 1706 (CO), 3406 (NH) (fig.109).

^{1}H-NMR (CF_3COOD): 2.20 (3H, t), 4.10 (2H, q), 6.20 (2H, m), 6.40 (2H, m), 7.00-8.30 (7H, m).

e: Brown crystals (82% yield), mp. 285 °C.

Analysis of $C_{23}H_{18}N_3O_3SCl$ (452). Calcd. %: C, 61.11; H, 4.01; N, 9.30; S, 7.10; Cl, 7.85. Found %: C, 61.24; H, 4.11; N, 9.21; S, 7.21; Cl, 7.93.

^{1}H-NMR (CF_3COOD): 2.20 (3H, t), 4.10 (2H, q), 6.20 (2H, m), 6.40 (2H, m), 7.00-8.30 (7H, m).

4-[2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-yl] semicarbazide (243_{a-e}).

General procedure: A mixture of **241_{a-e}** (0.01 mol) and hydrazine hydrate (10 ml) was refluxed for 1h. On cooling the solid product was filtered off, washed with ethanol and recrystallized from ethanol.

a: Brown crystals (70% yield), mp. 325 °C.

Analysis of $C_{23}H_{18}N_5O_2Cl$ (431.92). Calcd. %: C, 63.95; H, 4.20; N, 16.22; Cl, 8.22. Found %: C, 63.81; H, 4.14; N, 16.15; Cl, 8.30.

IR: 3350-3160 (NH_2), 3446 (NH), 1690 (CO) (fig.110). MS, m/z: 432 (fig.110).

^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.20-8.30 (13H, m).

b: Brown crystals (75% yield), mp. 246 °C.
Analysis of $C_{24}H_{20}N_5O_3Cl$ (461.95). Calcd. %: C, 62.40; H, 4.36; N, 15.16; Cl, 7.69. Found %: C, 62.55; H, 4.42; N, 15.29; Cl, 7.78.
^{1}H-NMR (CF_3COOD): 3.20 (3H, s), 5.10 (1H, s), 6.25-8.30 (12H, m) (fig.111).

c: Dark brown crystals (69% yield), mp. 261 °C.
Analysis of $C_{23}H_{17}N_6O_4Cl$ (476.93). Calcd. %: C, 57.92; H, 3.59; N, 17.63; Cl, 7.44. Found %: C, 57.79; H, 3.64; N, 17.74; Cl, 7.51.
IR: 3331-3230 (NH_2), 3440 (NH), 1690 (CO).

d: Dark brown crystals (78% yield), mp. > 340 °C.
Analysis of $C_{21}H_{16}N_5O_3Cl$ (421.89). Calcd. %: C, 59.78; H, 3.82; N, 16.60; Cl, 8.42. Found %: C, 59.64; H, 3.76; N, 16.47; Cl, 8.51.
IR: 3300-3200 (NH_2), 3435 (NH), 1670 (CO).
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.30-8.45 (11H, m).

e: Brown crystals (82% yield), mp. > 340 °C.
Analysis of $C_{21}H_{16}N_5O_2SCl$ (437.99). Calcd. %: C, 57.58; H, 3.68; N, 15.99; S, 7.33; Cl, 8.11. Found %: C, 57.46; H, 3.73; N, 15.82; S, 7.44; Cl, 8.20.
^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.30-8.40 (11H, m).

7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1",2":1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinolines (244_{a-e}).

General procedure: A solution of **241_{a-e}** (0.01 mol) in xylene (15 ml) was refluxed for one hour and then allowed to cool. The formed product was filtered off and recrystallized from ethanol.

a: Dark brown crystals (62% yield), mp. > 340 °C.
Analysis of $C_{23}H_{14}N_3O_2Cl$ (399.87). Calcd. %: C, 69.08; H, 3.53; N, 10.51; Cl, 8.88. Found %: C, 69.20; H, 3.61; N, 10.62; Cl, 8.77.

IR: 3385 (NH), 1690 (CO) (fig.112). MS, m/z: 400.10 (fig.112).

^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.45-8.25 (12H, m).

b: Brown crystals (65% yield), mp. 196 °C.

Analysis of $C_{24}H_{16}N_3O_3Cl$ (429.90). Calcd. %: C, 67.05; H, 3.75; N, 9.78; Cl, 8.26. Found %: C, 67.21; H, 3.82; N, 9.87; Cl, 8.32.

IR: 3391 (NH), 1690 (CO) (fig.113).

^{1}H-NMR (CF_3COOD): 3.30 (3H, s), 5.10 (1H, s), 6.40-8.30 (11H, m).

c: Brown crystals (61% yield), mp. > 340 °C.

Analysis of $C_{23}H_{13}N_4O_4Cl$ (444.87). Calcd. %: C, 62.09; H, 2.95; N, 12.60; Cl, 7.98. Found %: C, 62.23; H, 3.02; N, 12.74; Cl, 8.06.

IR: 3416 (NH), 1650 (CO) (fig.114).

^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.40-8.30 (11H, m).

d: Dark brown crystals (66% yield), mp. > 340 °C.

Analysis of $C_{21}H_{12}N_3O_3Cl$ (389.84). Calcd. %: C, 64.70; H, 3.10; N, 10.78; Cl, 9.11. Found %: C, 64.55; H, 3.19; N, 10.86; Cl, 9.26.

IR: 3380 (NH), 1705 (CO) (fig.115).

e: Pale brown crystals (69% yield), mp. > 340 °C.

Analysis of $C_{21}H_{12}N_3O_2SCl$ (405.94). Calcd. %: C, 62.13; H, 2.98; N, 10.35; S, 7.91; Cl, 8.75. Found %: C, 62.26; H, 2.87; N, 10.44; S, 7.83; Cl, 8.82.

IR: 3380 (NH), 1664 (CO) (fig.116).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.25-8.30 (10H, m).

7-Aryl-5,9-dichloropyrrolo[1",2":1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines (245_{a-e}).

General procedure: A suspension of $\mathbf{245_{a-e}}$ (0.01 mol) in phosphoryl chloride (25 ml) was heated under reflux for 4h. The reaction mixture was poured into ice-water, the residual solid product was worked up in an ammonium hydroxide-ice mixture, filtered, washed with water and recrystallized from benzene.

a: Brown crystals (70% yield), mp. 254 °C.

Analysis of $C_{23}H_{13}N_3OCl_2$ (418.36). Calcd. %: C, 66.03; H, 3.13; N, 10.05; Cl, 16.97. Found %: C, 66.17; H, 3.07; N, 10.14; Cl, 16.83.

^{1}H-NMR ($CDCl_3$): 5.10 (1H, s), 6.35-8.40 (12H, m).

b: Brown crystals (73% yield), mp. 242 °C.
Analysis of $C_{24}H_{15}N_3O_2Cl_2$ (448.39). Calcd. %: C, 64.28; H, 3.37; N, 9.37; Cl, 15.83. Found %: C, 64.39; H, 3.43; N, 9.45; Cl, 15.72.
^{1}H-NMR ($CDCl_3$): 3.30 (3H, s), 5.10 (1H, s), 6.30-8.40 (11H, m).

c: Dark brown crystals (68% yield), mp. 228 °C.
Analysis of $C_{23}H_{12}N_4O_3Cl_2$ (463.37). Calcd. %: C, 59.61; H, 2.61; N, 12.09; Cl, 15.32. Found %: C, 59.74; H, 2.56; N, 12.18; Cl, 15.20.
^{1}H-NMR ($CDCl_3$): 5.10 (1H, s), 6.30-8.40 (11H, m).

d: Dark brown crystals (74% yield), mp. 298 °C.
Analysis of $C_{21}H_{11}N_3O_2Cl_2$ (408.33). Calcd. %: C, 61.77; H, 2.72; N, 10.29; Cl, 17.39. Found %: C, 61.64; H, 2.68; N, 10.18; Cl, 17.27.
^{1}H-NMR ($CDCl_3$): 5.00 (1H, s), 6.25-8.30 (10H, m).

e: Brown crystals (77% yield), mp. 291 °C.
Analysis of $C_{21}H_{11}N_3OSCl_2$ (424.43). Calcd. %: C, 59.42; H, 2.61; N, 9.90; S, 7.56; Cl, 16.73. Found %: C, 59.31; H, 2.58; N, 9.82; S, 7.66; Cl, 16.60.
^{1}H-NMR ($CDCl_3$): 5.10 (1H, s), 6.25-8.30 (10H, m).

7-Aryl-5-chloro-9-hydrazinopyrrolo[1",2":1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines (246_{a-e}).

General procedure: A mixture of **245_{a-e}** (0.01 mol) and hydrazine hydrate (5 ml, 98%) in ethanol (25 ml) was heated under reflux for 5h. The product formed after cooling was filtered, washed with ethanol and recrystallized from dioxane.

a: Dark brown crystals (64% yield), mp. 294 °C.
Analysis of $C_{23}H_{16}N_5OCl$ (413.91). Calcd. %: C, 66.74; H, 3.90; N, 16.92; Cl, 8.58. Found %: C, 66.62; H, 3.20; N, 16.99; Cl, 8.66.
IR: 3324-3181 (NH_2), 3473 (NH) (fig.117). MS, m/z: 414.02 (fig.117).
^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.30-8.20 (12H, m).

b: Dark brown crystals (66% yield), mp. 282 °C.

Analysis of $C_{24}H_{18}N_5O_2Cl$ (443.93). Calcd. %: C, 64.93; H, 4.09; N, 15.78; Cl, 8.00. Found %: C, 64.80; H, 4.15; N, 15.91; Cl, 7.89.

IR: 3300-3195 (NH_2), 3416 (NH).

^{1}H-NMR (CF_3COOD): 3.30 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m).

c: Brown crystals (62% yield), mp. 257 °C.

Analysis of $C_{23}H_{15}N_6O_3Cl$ (458.91). Calcd. %: C, 60.19; H, 3.30; N,18.32; Cl, 7.74. Found %: C, 60.30; H, 3.41; N, 18.44; Cl, 7.81.

IR: 3315-3202 (NH_2), 3430 (NH).

^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.30-8.30 (11H, m).

d: Dark brown crystals (68% yield), mp. > 340 °C.

Analysis of $C_{21}H_{14}N_5O_2Cl$ (403.87). Calcd. %: C, 62.45; H, 3.49; N, 17.35; Cl, 8.79. Found %: C, 62.57; H, 3.57; N, 17.47; Cl, 8.87.

IR: 3300-3180 (NH_2), 3446 (NH).

e: Brown crystals (71% yield), mp. 95 °C.

Analysis of $C_{21}H_{14}N_5OSCl$ (419.97). Calcd. %: C, 60.05; H, 3.36; N, 16.68; S, 7.64; Cl, 8.45. Found %: C, 60.15; H, 3.42; N, 16.81; S, 7.58; Cl, 8.38.

IR: 3310-3165 (NH_2), 3450 (NH).

^{1}H-NMR (CF_3COOD): 5.00 (1H, s), 6.20-8.25 (10H, m).

7-Aryl-5-chloro-9-methyl[1,2,4]triazolo[3",4":3',4']pyrrolo-[1",2":1',2']pyrazino[5',6':5,6] pyrano[3,2-h]quinolines (247_{a-e}).

General procedure: A solution of **246_{a-e}** (0.01 mol) in acetic acid (30 ml) was heated under reflux for 6h. the reaction mixture was concentrated in vacuo and the solid product was collected , washed with water and recrystallized from acetic acid.

a: Brown crystals (55% yield), mp. 118°C.

Analysis of $C_{25}H_{16}N_5OCl$ (437.93). Calcd. %: C, 68.56; H, 3.68; N, 16.00; Cl, 8.11. Found %: C, 68.45; H, 3.73; N, 16.06; Cl, 8.19.

IR: 2925 (CH aliph.) (fig.118).

^{1}H-NMR ($CDCl_3$): 2.10 (3H, s), 5.10 (1H, s), 6.30-8.10 (12H, m).

b: Brown crystals (58% yield), mp. 234 °C.

Analysis of $C_{26}H_{18}N_5O_2Cl$ (467.95). Calcd. %: C, 66.73; H, 3.88; N, 14.97; Cl, 7.59. Found %: C, 66.60; H, 3.93; N, 14.86; Cl, 7.48.
^{1}H-NMR ($CDCl_3$): 2.10 (3H, s), 3.20 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m) (fig.119).

c: Brown crystals (54% yield), mp. 257 °C.
Analysis of $C_{25}H_{15}N_5O_3Cl$ (468.92). Calcd. %: C, 64.03; H, 3.22; N, 14.94; Cl, 7.57. Found %: C, 64.13; H, 3.16; N, 14.84; Cl, 7.66.
^{1}H-NMR ($CDCl_3$): 2.10 (3H, s), 5.10 (1H, s), 6.30-8.20 (11H, m).

d: Brown crystals (60% yield), mp. > 340 °C.
Analysis of $C_{23}H_{14}N_5O_2Cl$ (427.89). Calcd. %: C, 64.56; H, 3.30; N, 16.37; Cl, 8.30. Found %: C, 64.43; H, 3.24; N, 16.25; Cl, 8.43.
^{1}H-NMR ($CDCl_3$): 2.10 (3H, s), 5.00 (1H, s), 6.20-8.35 (10H, m).

e: Brown crystals (63% yield), mp. 195 °C.
Analysis of $C_{23}H_{14}N_5OSCl$ (443.99). Calcd. %: C, 62.22; H, 3.18; N, 15.78; S, 7.23; Cl, 8.00. Found %: C, 62.36; H, 3.25; N, 15.67; S, 7.17; Cl, 8.11.
^{1}H-NMR ($CDCl_3$): 2.10 (3H, s), 5.00 (1H, s), 6.20-8.30 (10H, m).

7-Aryl-5-chloro-9-thioxo-7,10-dihydro[1,2,4]triazolo[3",4":3',4']-pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines (248_{a-e}).

General procedure: A mixture of **246_{a-e}** (0.01 mol) carbon disulfide (3 ml) in ethanol (30 ml) and two pellets of potassium hydroxide was heated under reflux on a water bath for 6h. The solid product obtained was dissolved in water then acidified with acetic acid and recrytallized from dioxane.

a: Brown crystals (59% yield), mp. 191 °C.
Analysis of $C_{24}H_{14}N_5OSCl$ (456). Calcd. %: C, 63.21; H, 3.10; N, 15.36; S, 7.04; Cl, 7.79. Found %: C, 63.32; H, 3.01; N, 15.45; S, 7.13; Cl, 7.88.
IR: 3222 (NH), 1190 (CS) (fig.12). MS, m/z: 456.02 (fig.120).
^{1}H-NMR (CF_3COOD): 5.10 (1H, s), 6.30-8.25 (12H, m).

b: Brown crystals (62% yield), mp. > 340 °C.
Analysis of $C_{25}H_{16}N_5O_2SCl$ (486.03). Calcd. %: C, 61.78; H, 3.32; N, 14.41; S, 6.61; Cl, 7.30. Found %: C, 61.89; H, 3.38; N, 14.32; S, 6.62; Cl, 7.41.

^1H-NMR (CF_3COOD): 3.50 (3H, s), 5.10 (1H, s), 6.30-8.30 (11H, m).

c: Brown crystals (58% yield), mp. 263 °C.

Analysis of $C_{24}H_{13}N_6O_3SCl$ (501). Calcd. %: C, 57.53; H, 2.62; N, 16.78; S, 6.41; Cl, 7.09. Found %: C, 7.43; H, 2.56; N, 16.86; S, 6.50; Cl, 7.19.

IR: 3350 (NH), 1190 (CS).

d: Brown crystals (65% yield), mp. 127 °C.

Analysis of $C_{22}H_{12}N_5O_2SCl$ (445.97). Calcd. %: C, 59.25; H, 2.71; N, 15.71; S, 7.20; Cl, 7.96. Found %: C, 59.37; H, 2.65; N, 15.62; S, 7.12; Cl, 7.84.

IR: 3325 (NH), 1195 (CS).

^1H-NMR ($CDCl_3$): 5.10 (1H, s), 6.20-8.30 (10H, m).

e: Brown crystals (67% yield), mp. > 340 °C.

Analysis of $C_{22}H_{12}N_5OS_2Cl$ (462.07). Calcd. %: C, 57.18; H, 2.62; N, 15.16; S, 13.89; Cl, 7.68. Found %: C, 57.29; H, 2.56; N, 15.24; S, 13.78; Cl, 7.57.

IR: 3340 (NH), 1180 (CS).

^1H-NMR (CF_3COOD): 5.10 (1H, s), 6.20-8.30 (10H, m).

List of Compounds

List of new compounds	Compd. No.
1- 2-Amino-4-aryl-6-chloro-3-cyano-4H-pyrano[3,2-h]quinolines	218_{a-e}
2- Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate	219_{a-e}
3- 7-Aryl-5-chloro-10-methyl-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]-pyrano[3,2-h]quinolines	220_{a-e}
4- 8-Amino-7-aryl-5-chloro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]quinolines	221_{a-e}
5- 7-Aryl-5-chloro-8-oxo-8,9-dihydro-7H-pyrimido[4',5':6,5]pyrano[3,2-h]-quinolines	222_{a-e}
6- 4-Aryl-6-chloro-3-cyano-2-(ethoxymethylenamino)-4H-pyrano[3,2-h]-quinolines	223_{a-e}
7- 7-Aryl-5-chloro-8-imino-9-phenyl-7H-pyrimido[4',5':6,5]pyrano[3,2-h]-quinolines	224_{a-e}
8- 8-Amino-7-aryl-5-chloro-9-cyano-10-oxo-pyrido[2',3':6,5]pyrano[3,2-h]-quinolines	225_{a-e}
9- 5-Aryl-4,7-dichloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]quinolines	226_{a-e}
10- 2-Amino-4-aryl-3-(4',5'-dihydro-1H-imidazol-2-yl)pyrano[3,2-h]-quinolines	227_{a-e}
11- 2,3,14-Trihydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinolines	228_{a-e}
12- 2,3,5,6,14-Pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano-[3,2-h]quinolines	229_{a-e} – 232_{a-e}
13- 5-Thioxo-2,3,6,14-tetrahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano-[3,2h]quinolines	233_{a-e}
14- 5-Aryl-7-chloro-4-hydrazino[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines	234_{a-e}
15- 14-Aryl-12-chloro[1,2,4]triazolo[3",4"-f][1,2,3]triazino[4',5':6,5]pyrano-[3,2-h]quinolines	235_{a-e}
16- 14-Aryl-12-chloro-3-thioxo[1,2,4]triazolo[3",4"-f][1,2,3]triazino-[4',5':6,5]pyrano[3,2-h]quinolines	236_{a-e}
17- 5-Aryl-4-azido-7-chloro[1,2,3]triazino[4',5':6,5]pyrano[3,2-h]-quinolines	237_{a-e}
18- Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylates	238_{a-e}
19- 2-(1-pyrrolyl)-4aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbohydrazide	239_{a-e}
20- 2-(1-Pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines	240_{a-e}
21- 2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-oylazid	241_{a-e}
22- Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbamate	242_{a-e}
23- 4-[2-(1-Pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-yl]-semicarbazide	243_{a-e}
24- 7-Aryl-5-chloro-9-oxo-7,8-dihydropyrrolo[1",2":1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinolines	244_{a-e}
25- 7-Aryl-5,9-dichloropyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano-[3,2-h]quinolines	245_{a-e}
26- 7-Aryl-5-chloro-9-hydrazinopyrrolo[1",2":1',2']pyrazino[5',6':5,6]-pyrano[3,2-h]quinolines	246_{a-e}

27- 7-Aryl-5-chloro-9-methyl[1,2,4]triazolo[3",4":3',4']pyrrolo[1",2":1',2']-
pyrazino[5',6':5,6] pyrano[3,2-h]quinolines 247_{a-e}

28- 7-Aryl-5-chloro-9-thioxo-7,10-dihydro[1,2,4]triazolo[3",4":3',4']-
pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinolines 248_{a-e}

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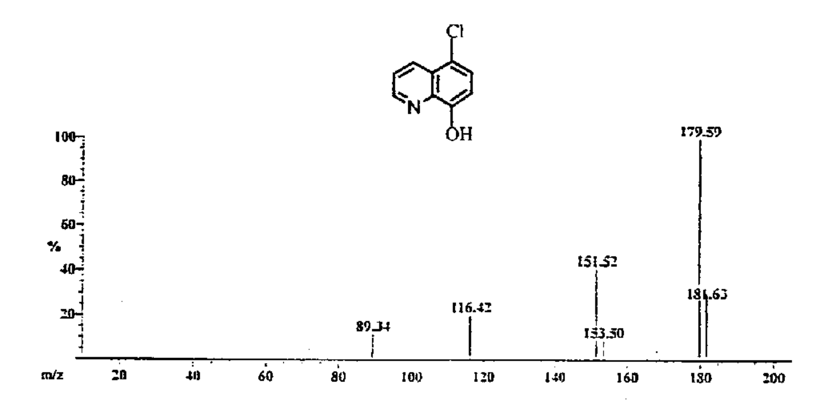
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Appendix



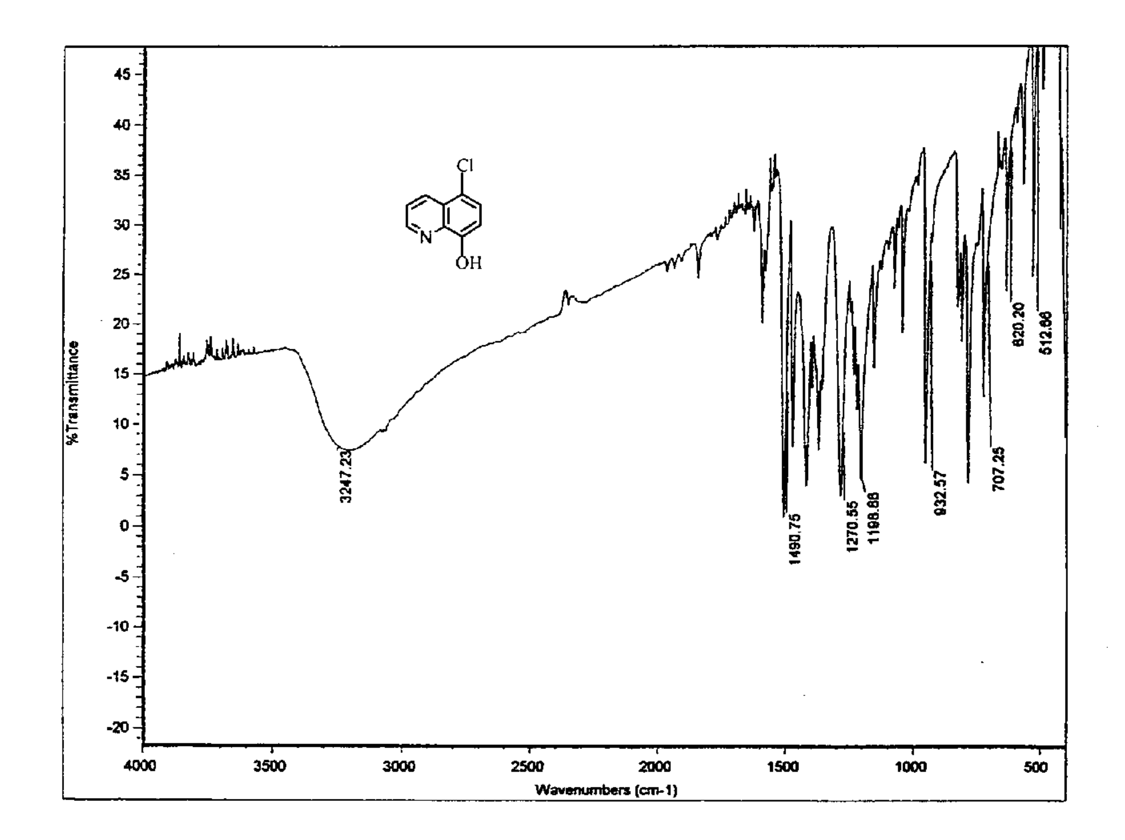


Fig.(1): 5-Chloro-8-quinolinol **(217)**.

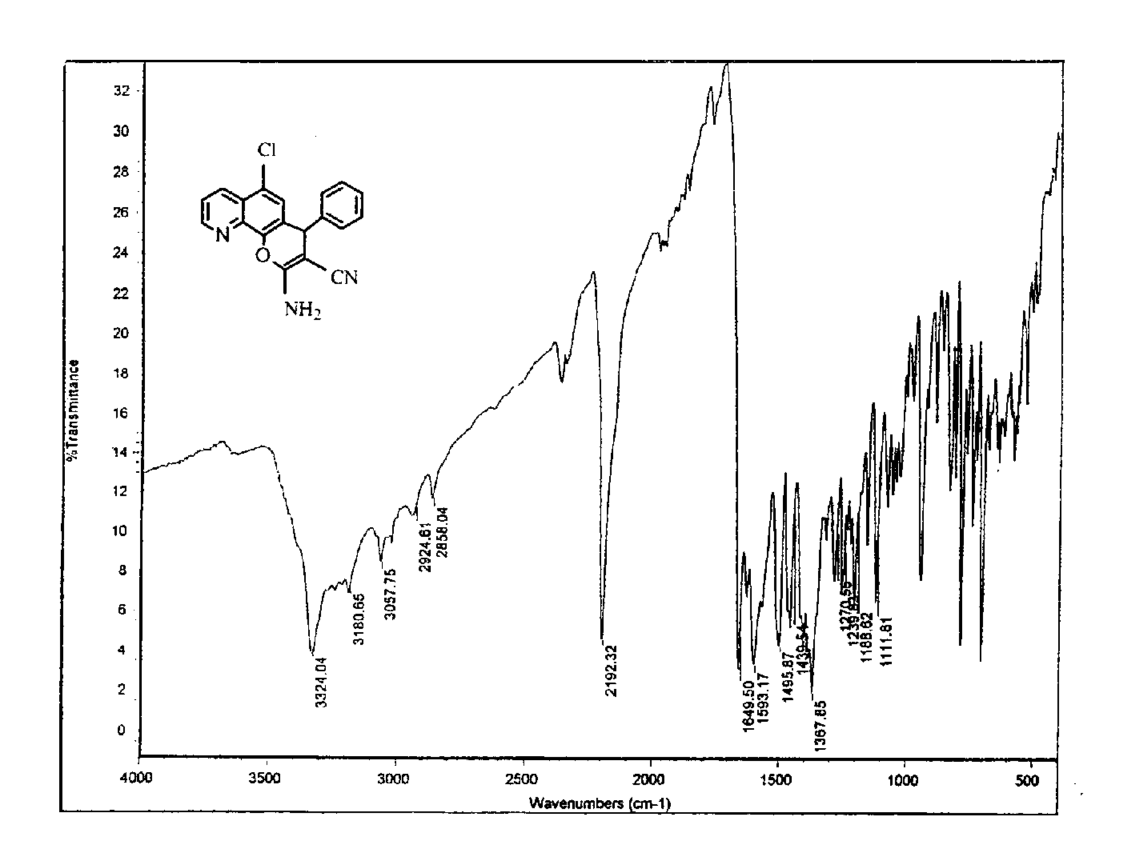
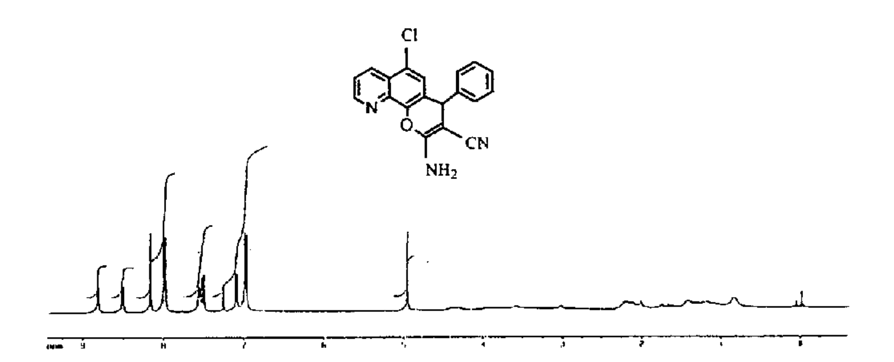


Fig.(2): 2-Amino-6-chloro-3-cyano-4-phenyl-4H-pyrano[3,2-h]quinoline **(218a)**.



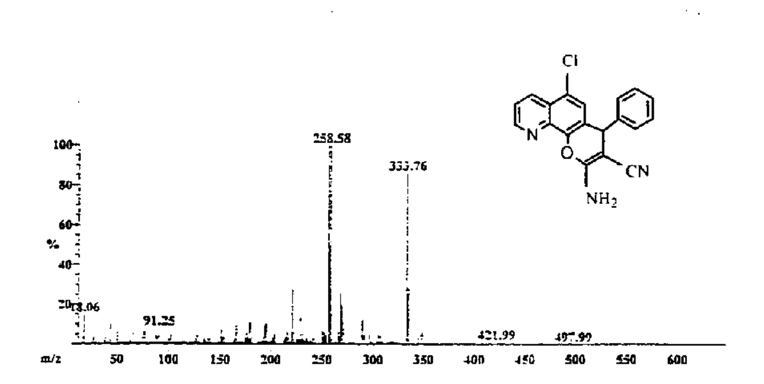


Fig.(3): 2-Amino-6-chloro-3-cyano-4-phenyl-4H-pyrano[3,2-h]quinoline **(218_a)**.

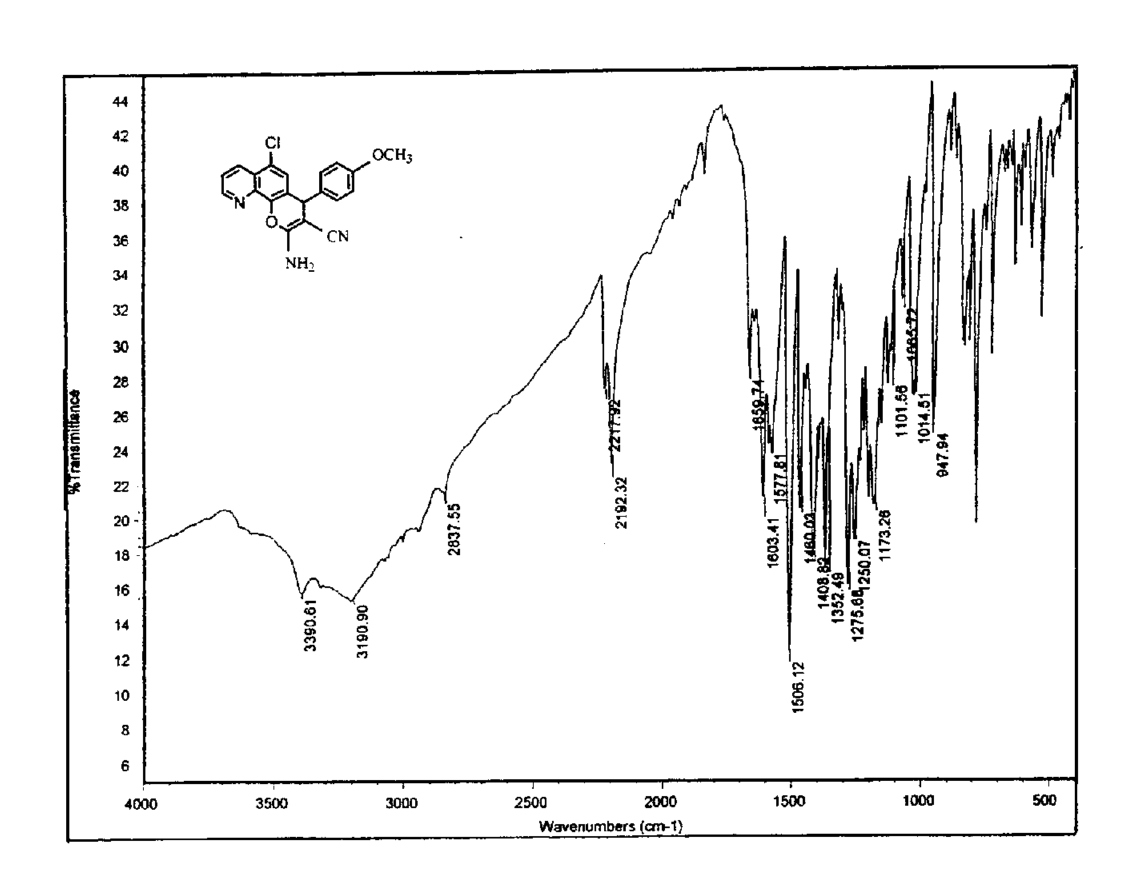


Fig.(4): 2-Amino-6-chloro-3-cyano-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline **(218_b)**.

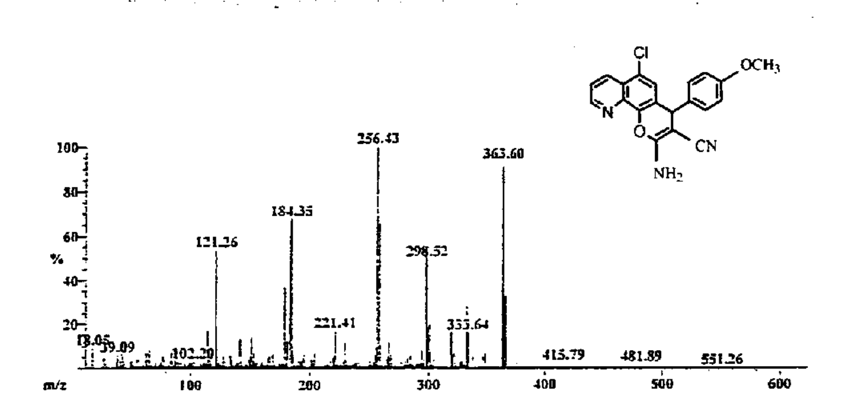


Fig.(5): 2-Amino-6-chloro-3-cyano-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline **(218$_b$)**.

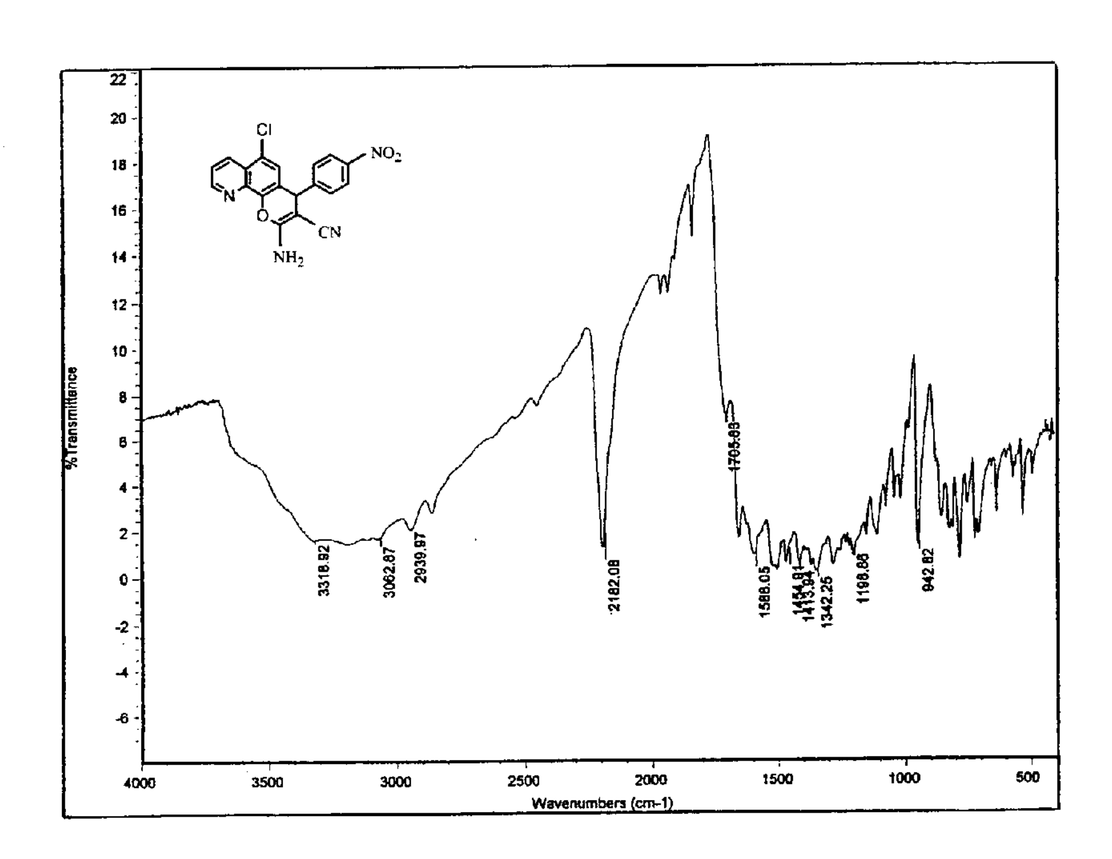
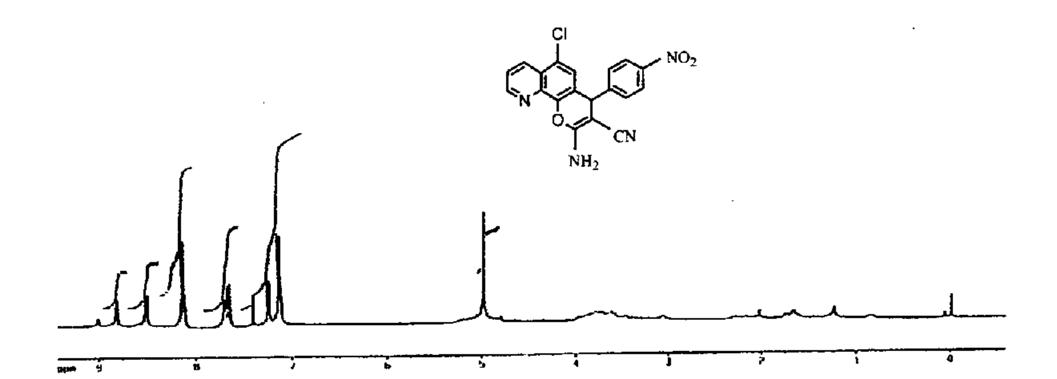


Fig.(6): 2-Amino-6-chloro-3-cyano-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline **(218_c)**.



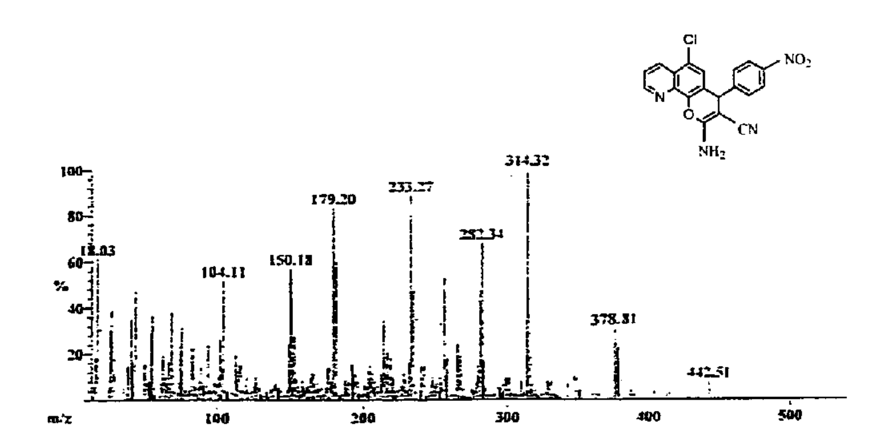
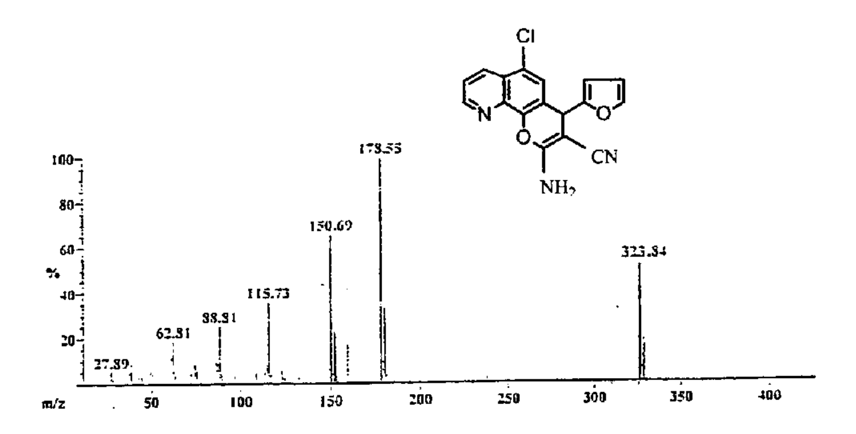


Fig.(7): 2-Amino-6-chloro-3-cyano-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline **(218_c)**.



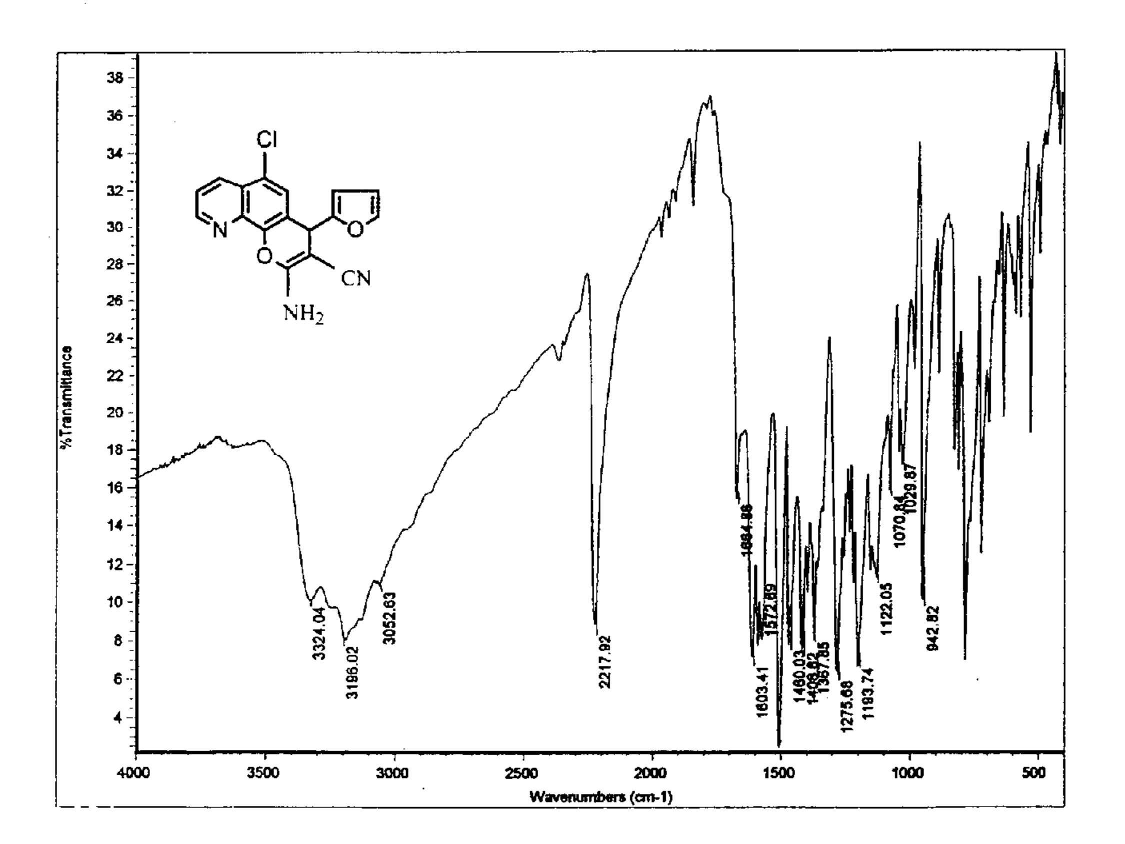
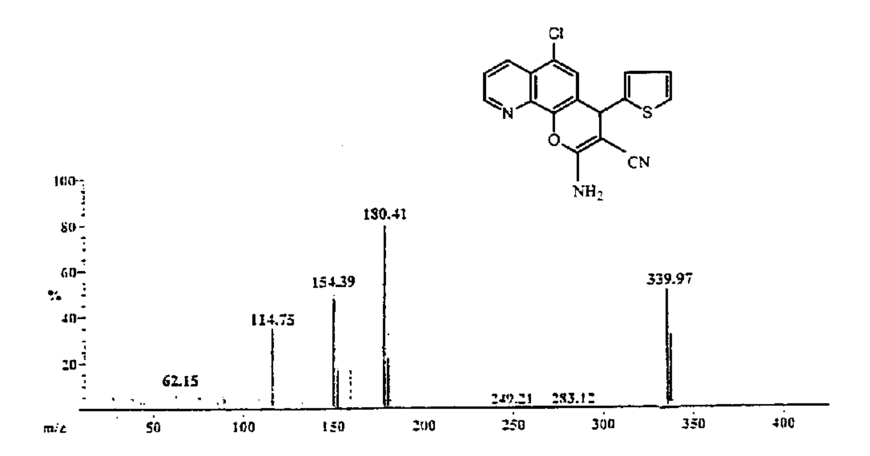


Fig.(8): 2-Amino-6-chloro-3-cyano-4-furyl-4H-pyrano[3,2-h]quinoline **(218_d)**.



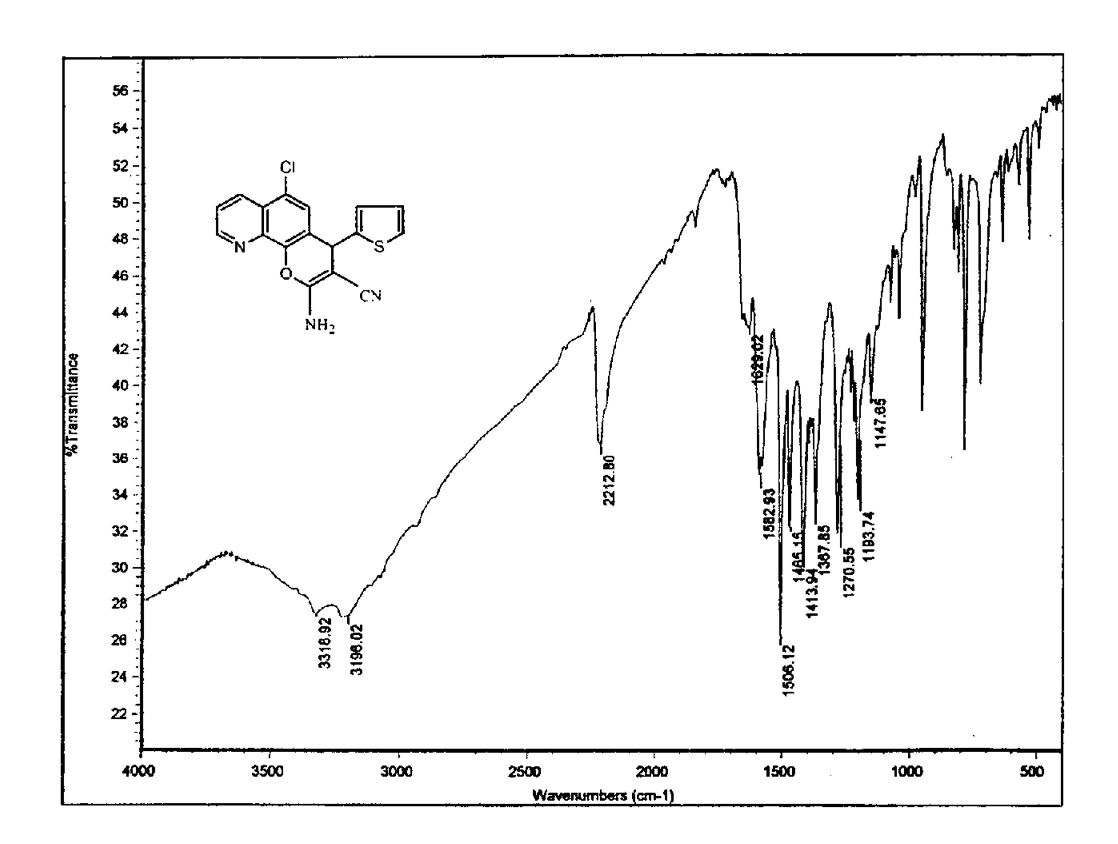


Fig.(9): 2-Amino-6-chloro-3-cyano-4-thienyl-4H-pyrano[3,2-h]quinoline **(218_e)**.

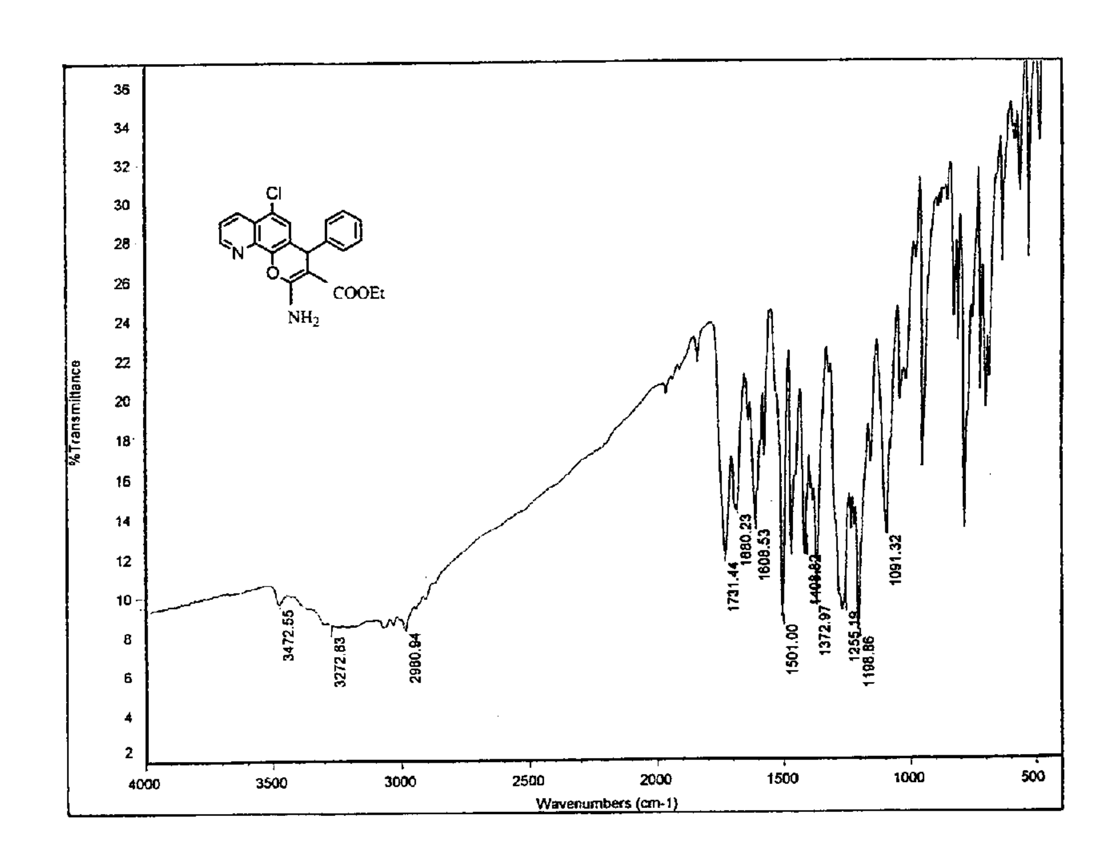


Fig.(10): Ethyl 2-amino-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219$_a$**).

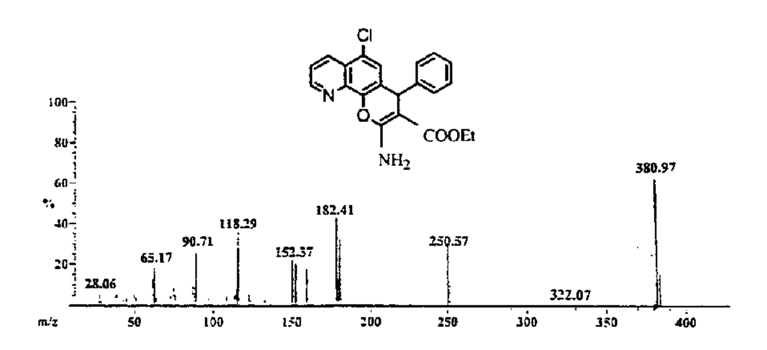


Fig.(11): Ethyl 2-amino-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate (**219_a**).

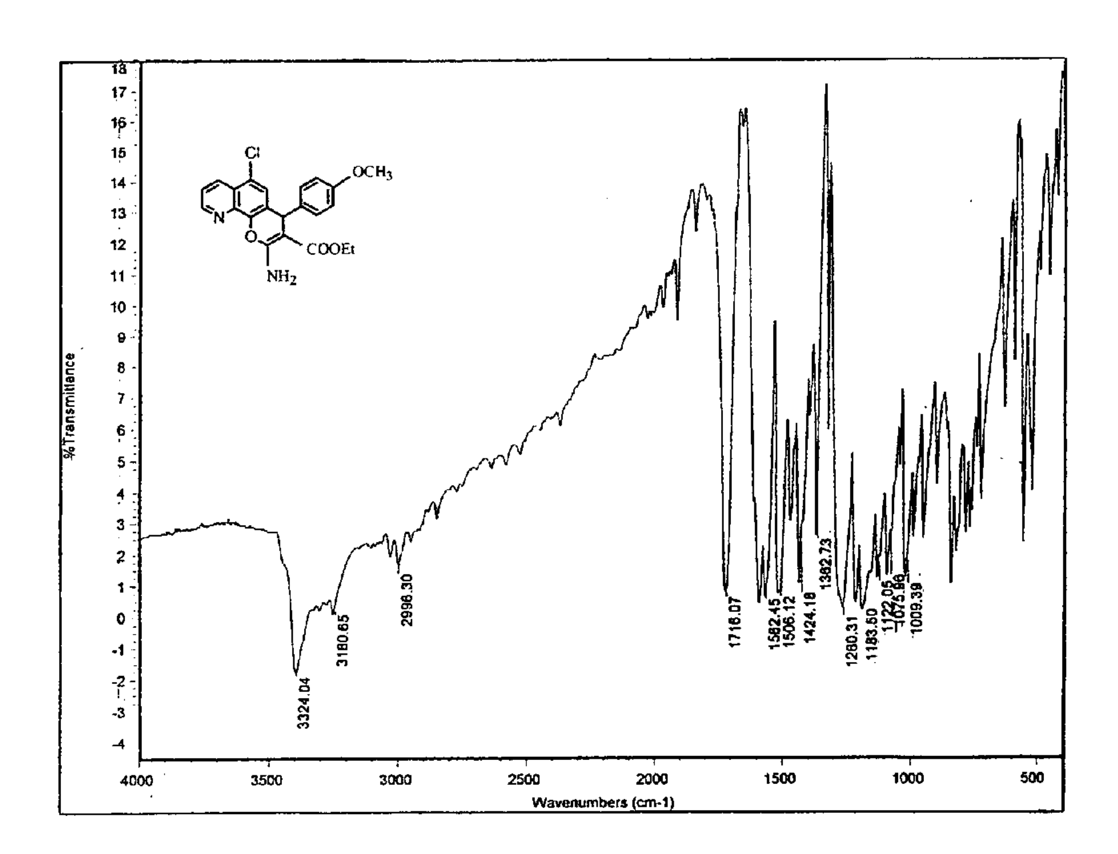


Fig.(12): Ethyl 2-amino-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate **(219_b)**.

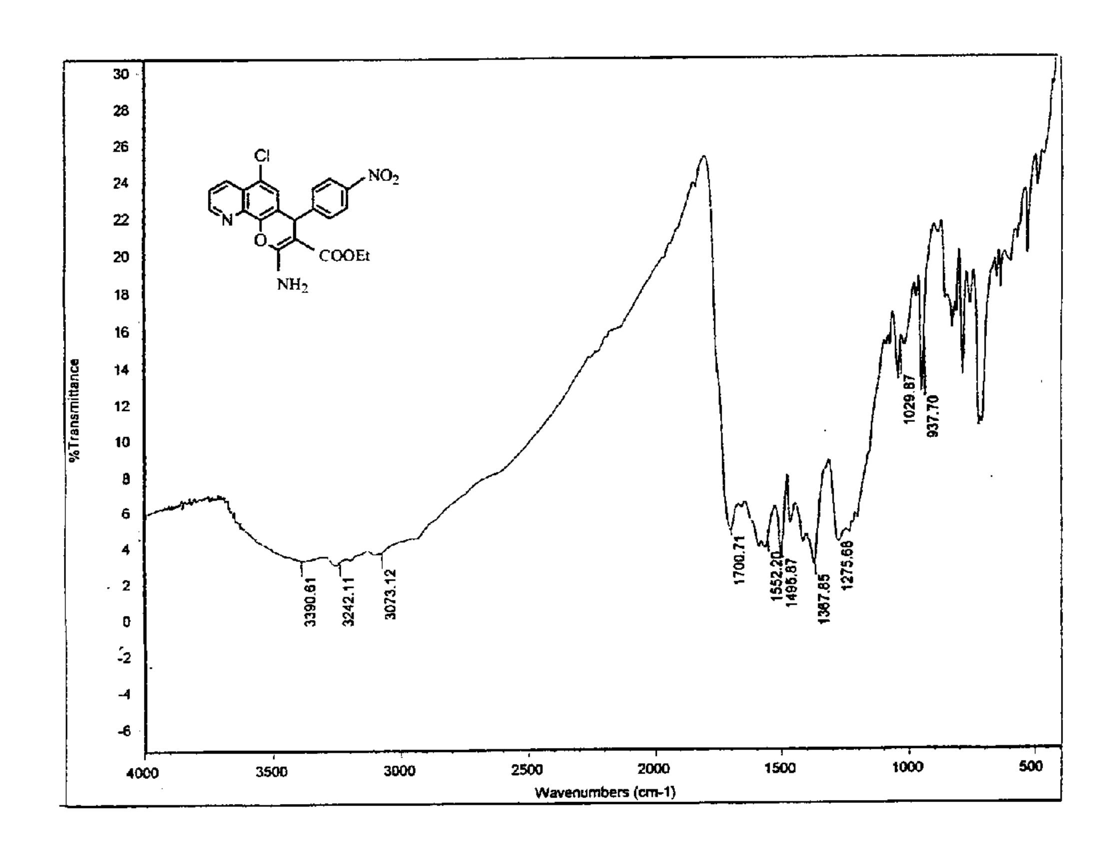


Fig.(13): Ethyl 2-amino-6-chloro-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate **(219_c)**.

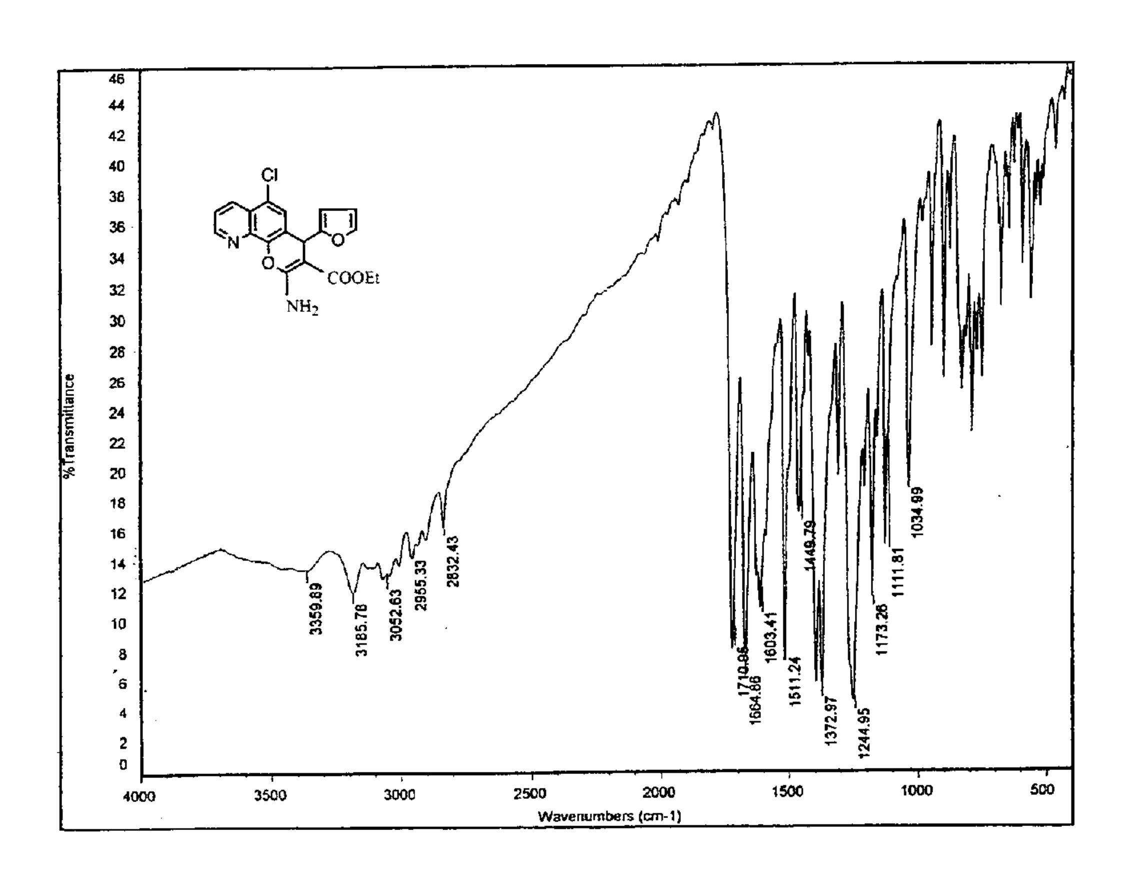


Fig.(14): Ethyl 2-amino-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(219_d)**.

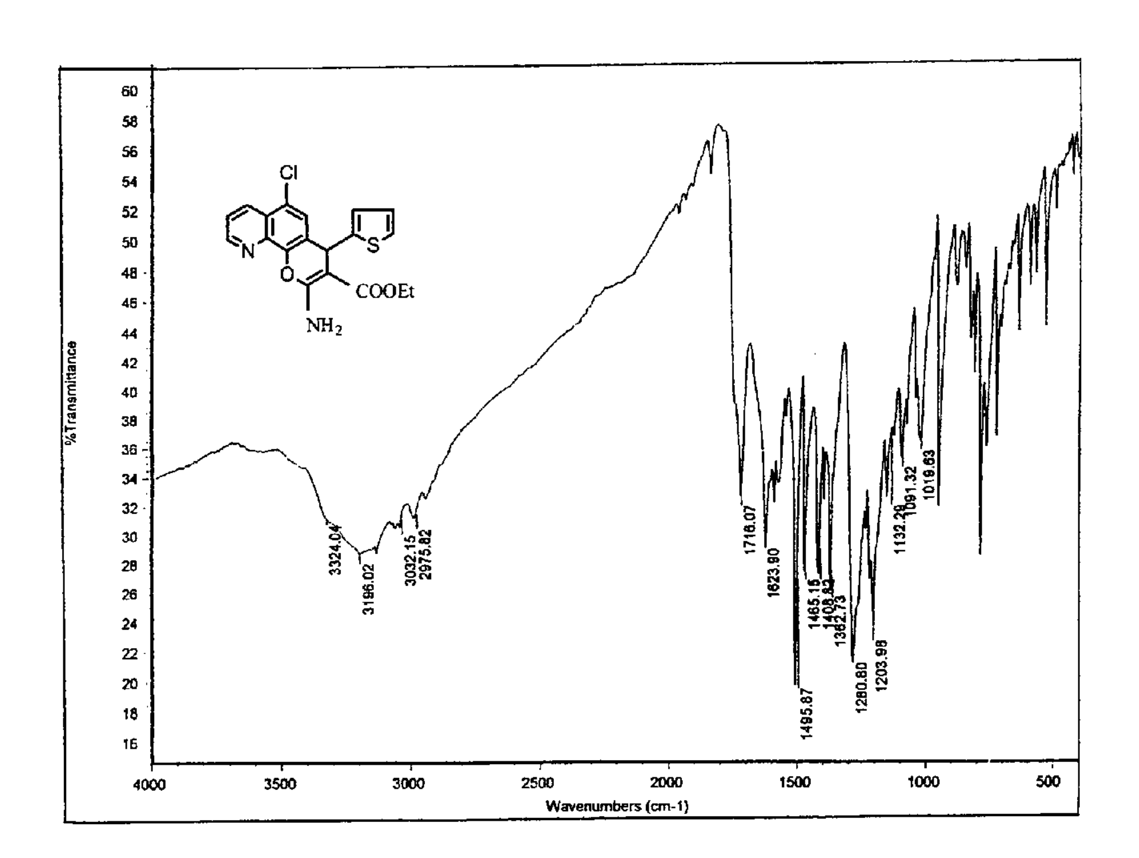
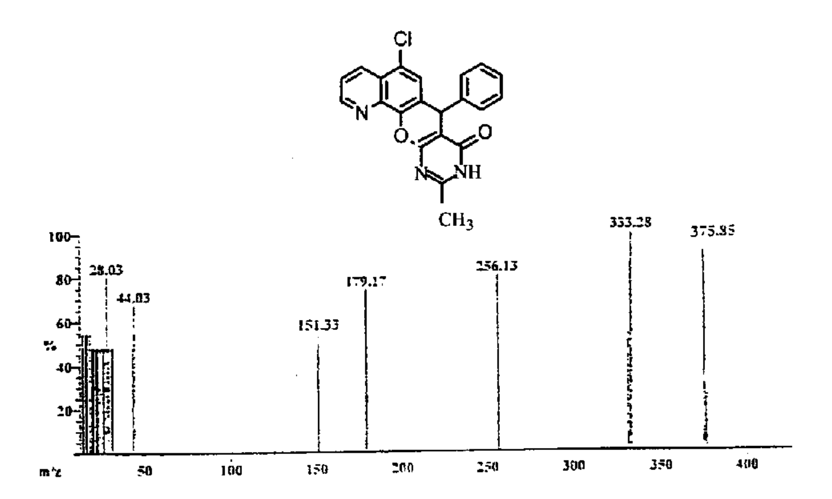


Fig.(15): Ethyl 2-amino-6-chloro-4-thienyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(219$_e$)**.



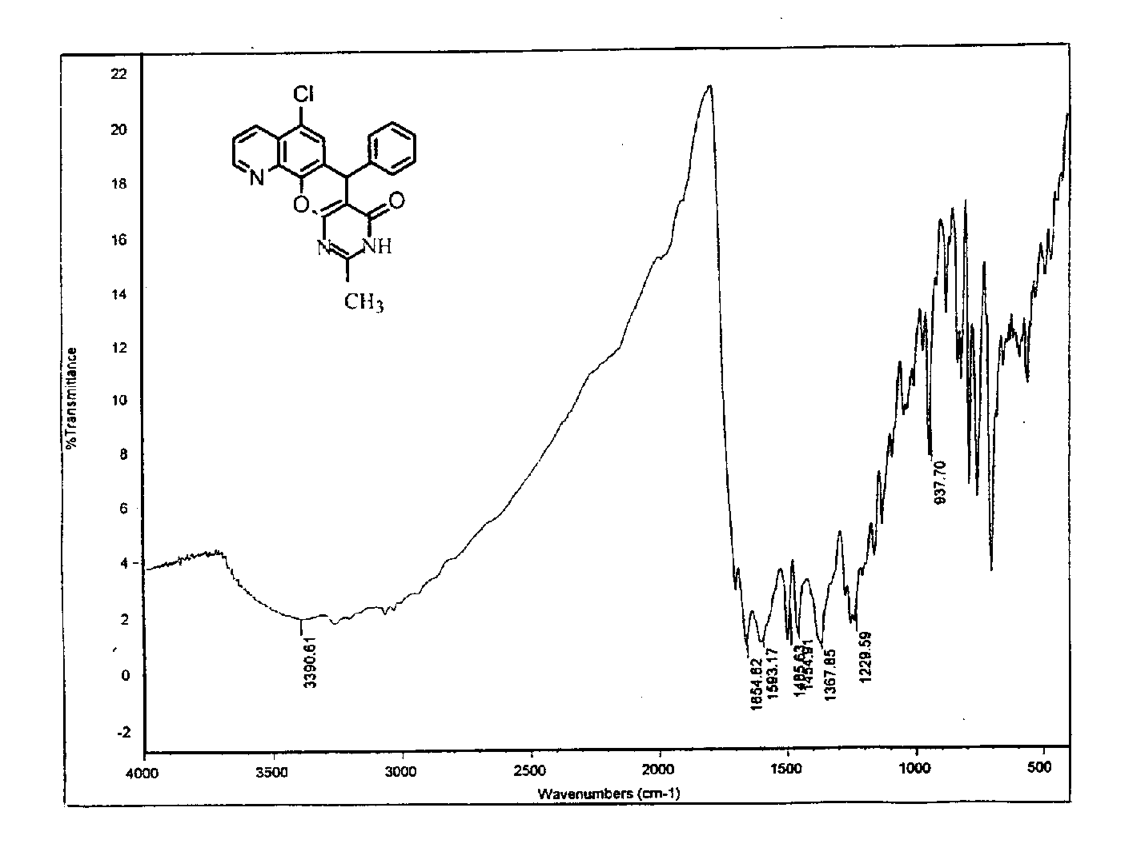
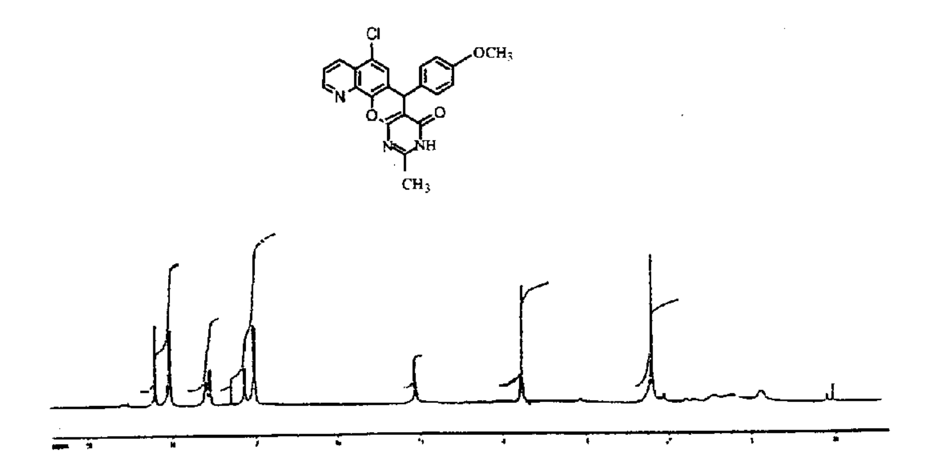


Fig.(16): 5-Chloro-10-methyl-7-phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]-pyrano[3,2-h]quinoline **(220$_a$)**.



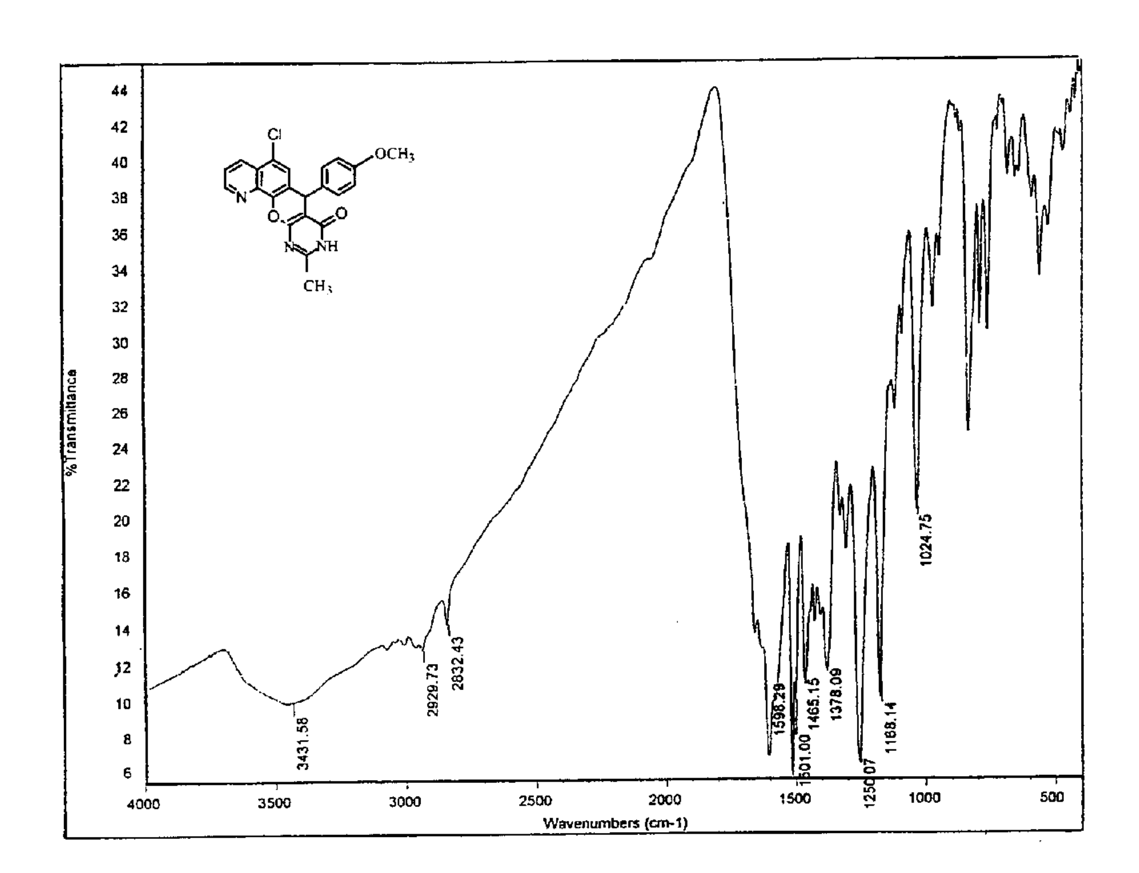
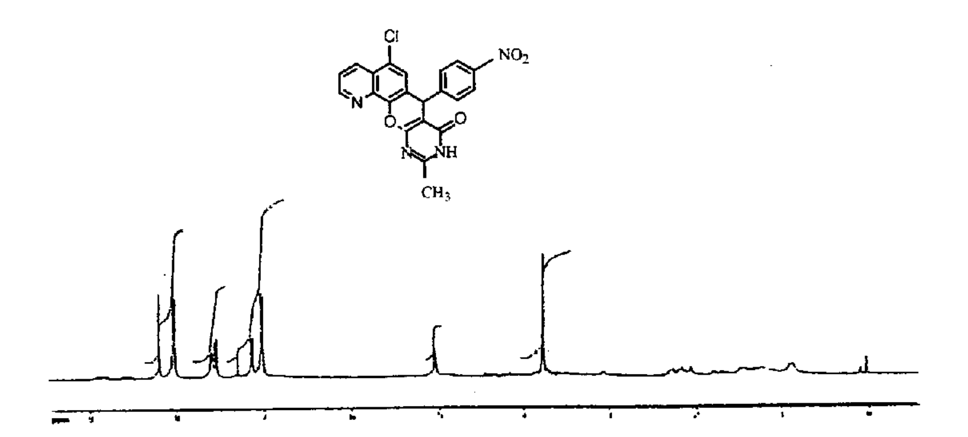


Fig.(17): 5-Chloro-10-methyl-7-(4-methoxy)phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(220_b)**.



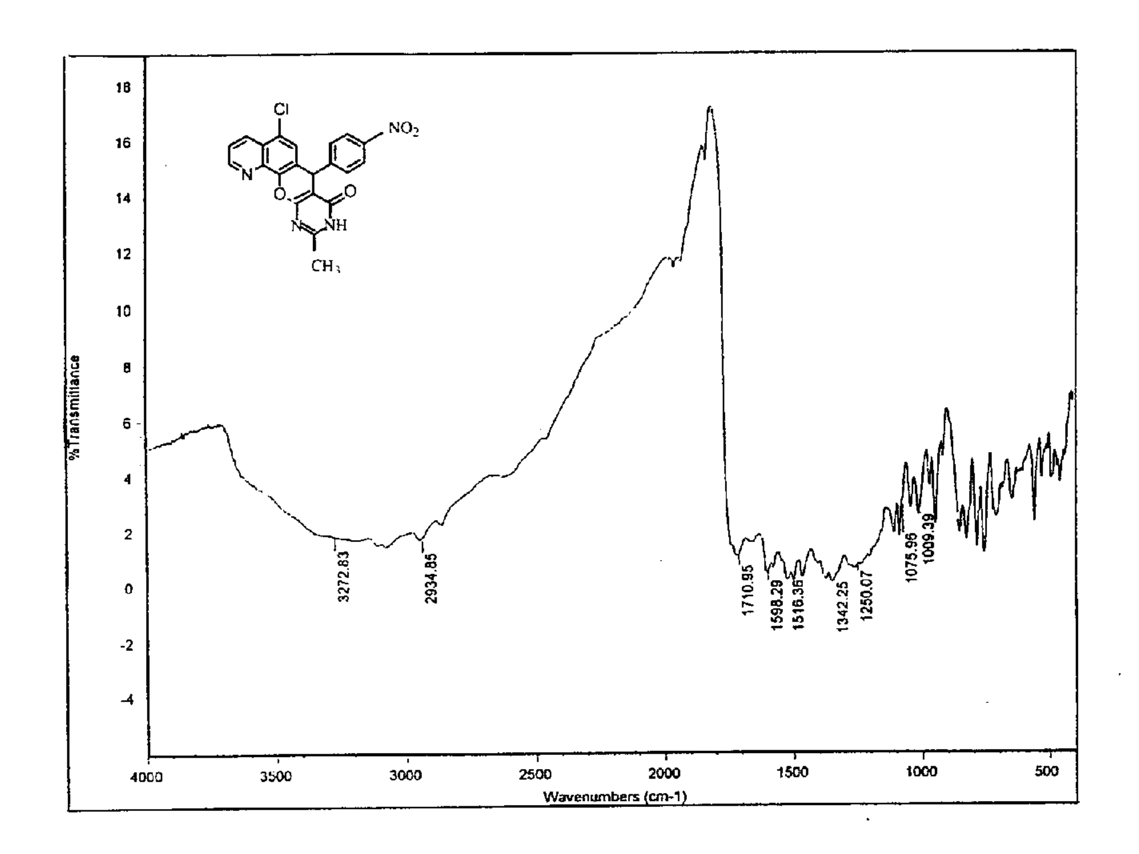


Fig.(18): 5-Chloro-10-methyl-7-(4-nitro)phenyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline **(220$_c$)**.

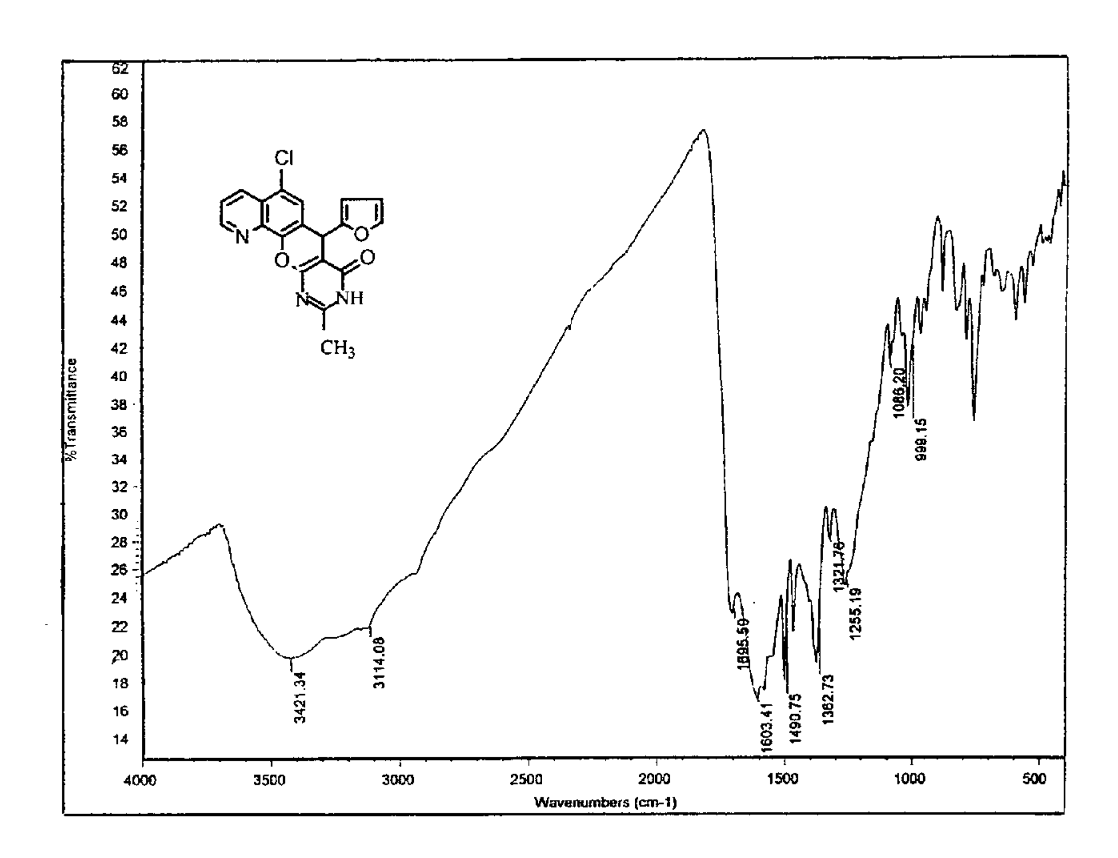


Fig.(19): 5-Chloro-10-methyl-7-furyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline **(220d)**.

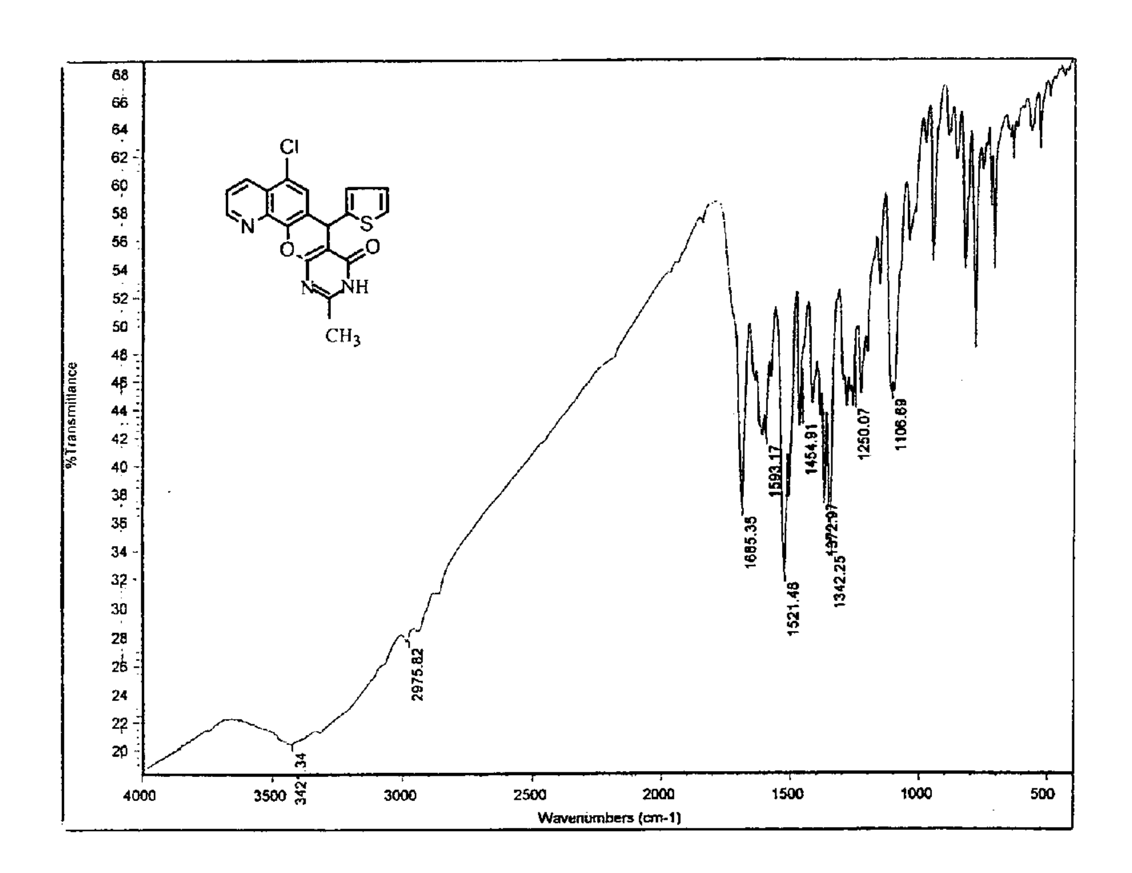
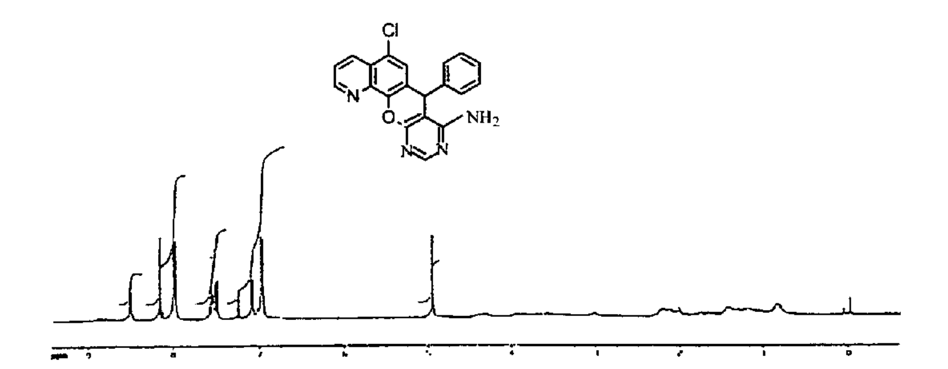


Fig.(20): 5-Chloro-10-methyl-7-thienyl-7H-8-oxo-8,9-dihydropyrimido-[4',5':6,5]pyrano[3,2-h]quinoline **(220_e)**.



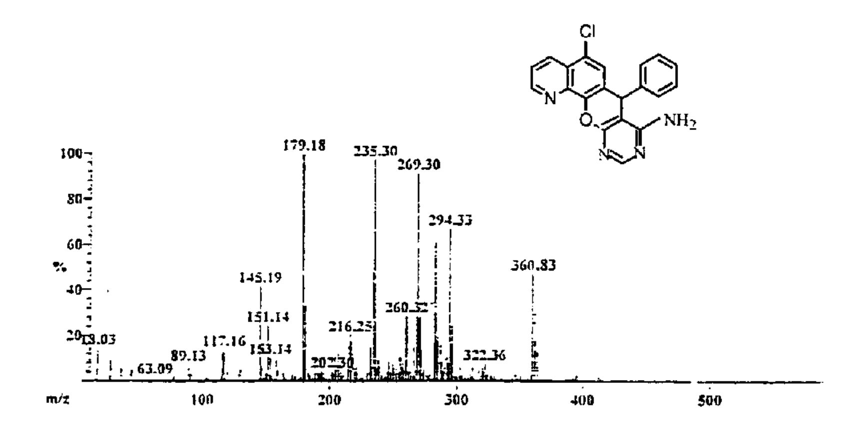


Fig.(21): 8-Amino-5-chloro-7-phenyl-7H-pyrimido[4',5':6,5]pyrano-[3,2-h]quinoline **(221$_a$)**.

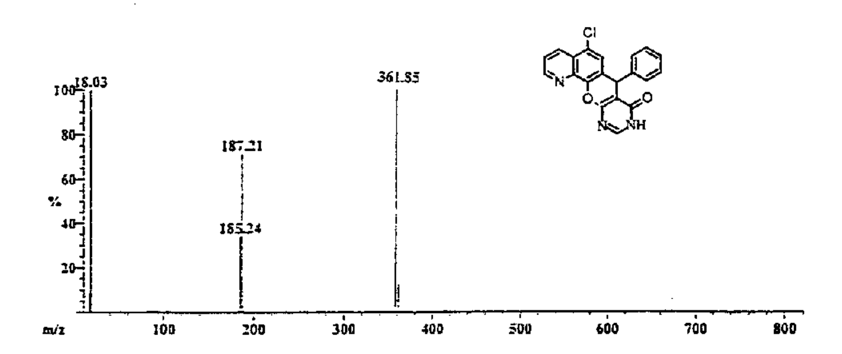


Fig.(22): 5-Chloro-7-phenyl-7H-8-oxo-8,9-dihydropyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**222_a**).

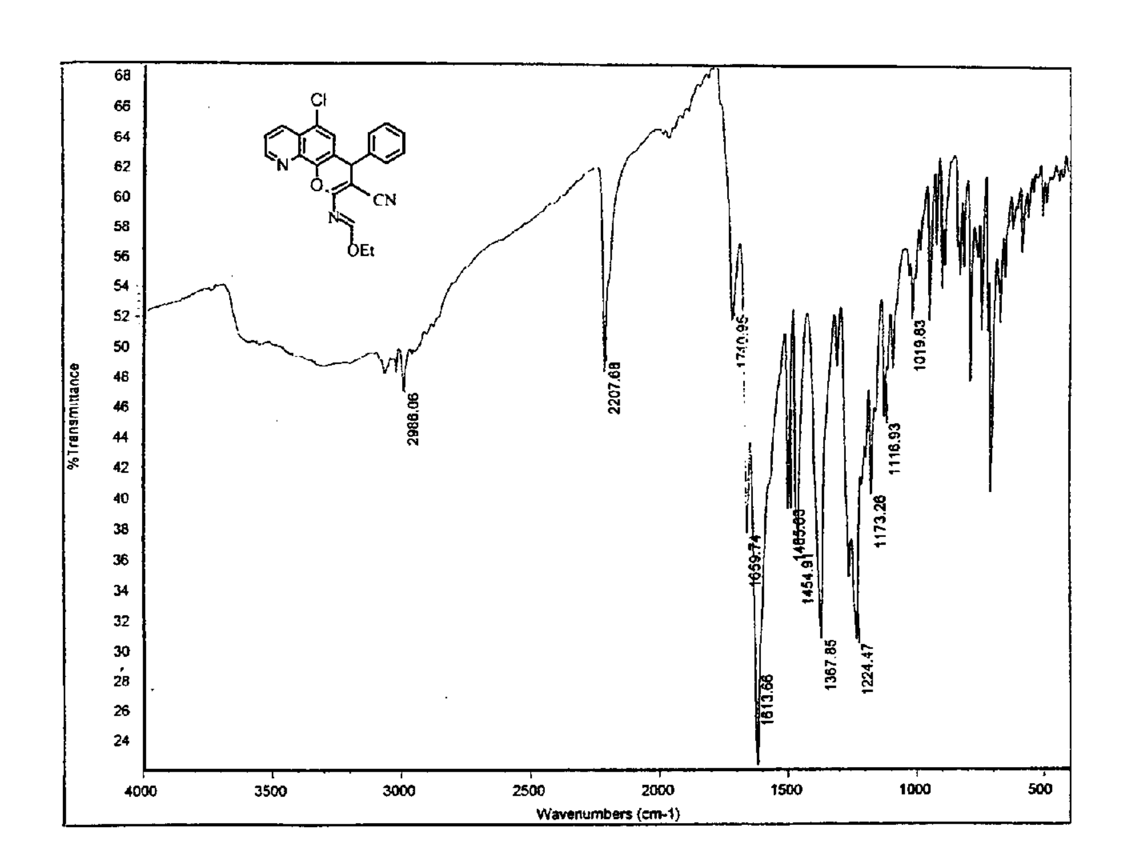


Fig.(23): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-phenyl-4H-pyrano-[3,2-h]quinoline **(223_a)**.

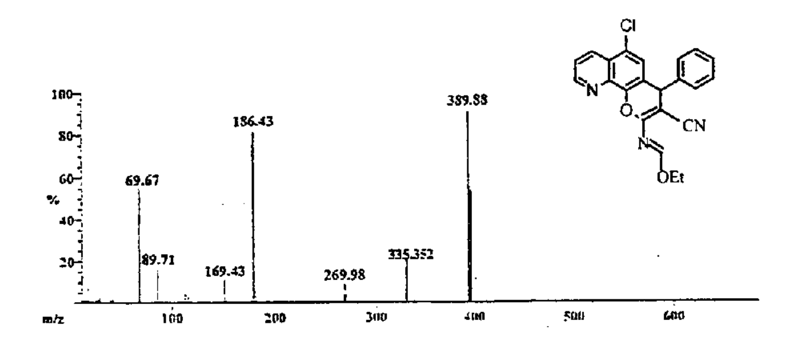


Fig.(24): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-phenyl-4H-pyrano-[3,2-h]quinoline **(223_a)**.

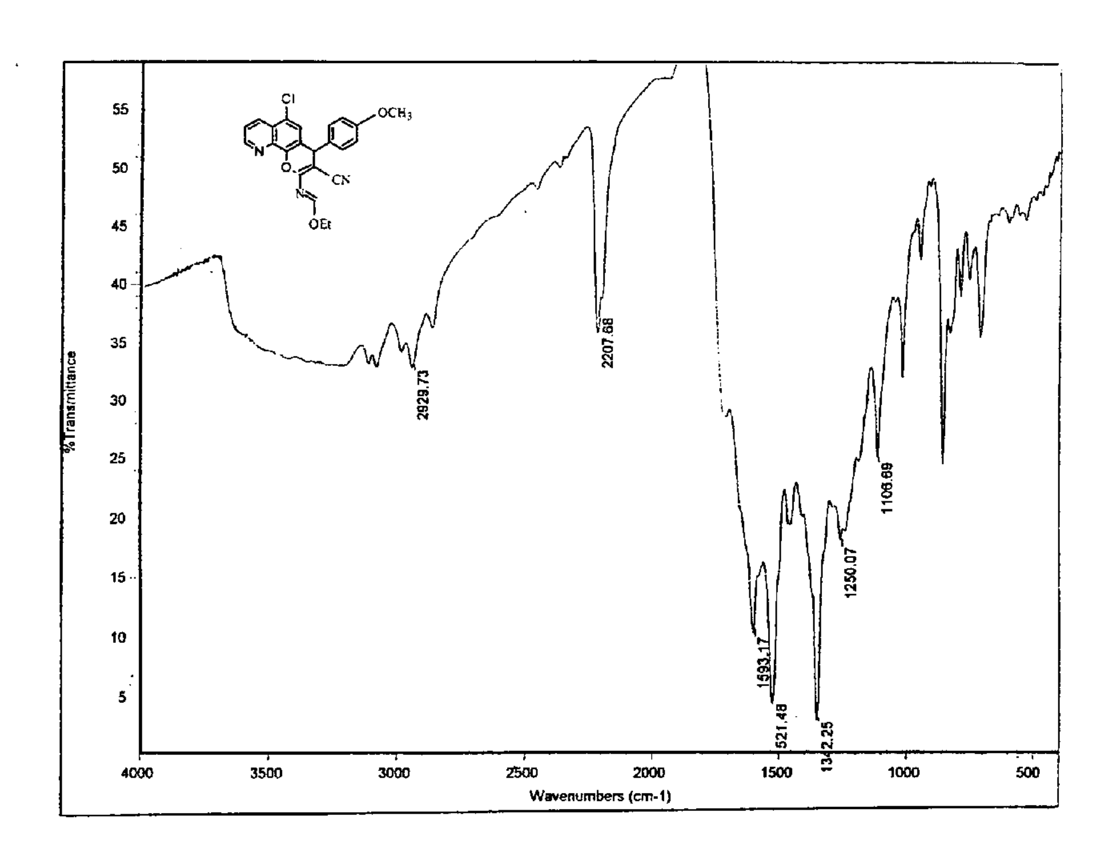


Fig.(25): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-(4-methoxy)phenyl-4H-pyrano[3,2-h]quinoline (**223_b**).

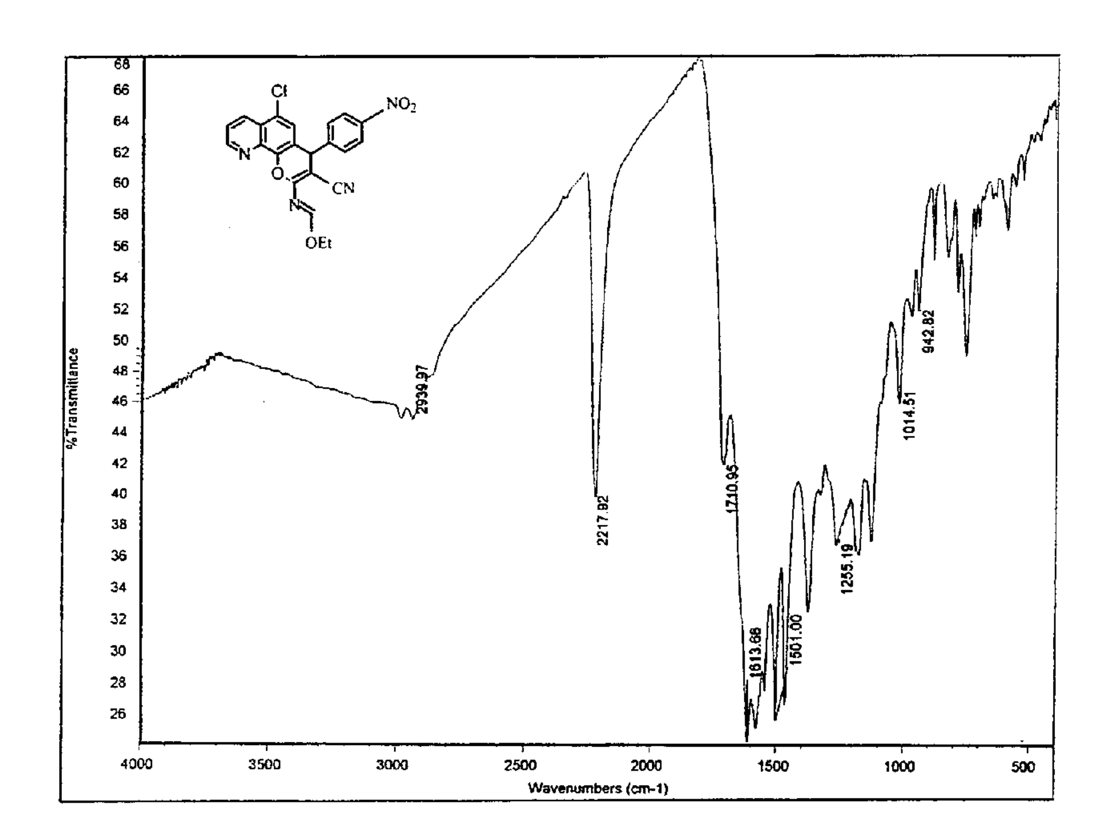


Fig.(26): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-(4-nitro)phenyl-4H-pyrano[3,2-h]quinoline **(223_c)**.

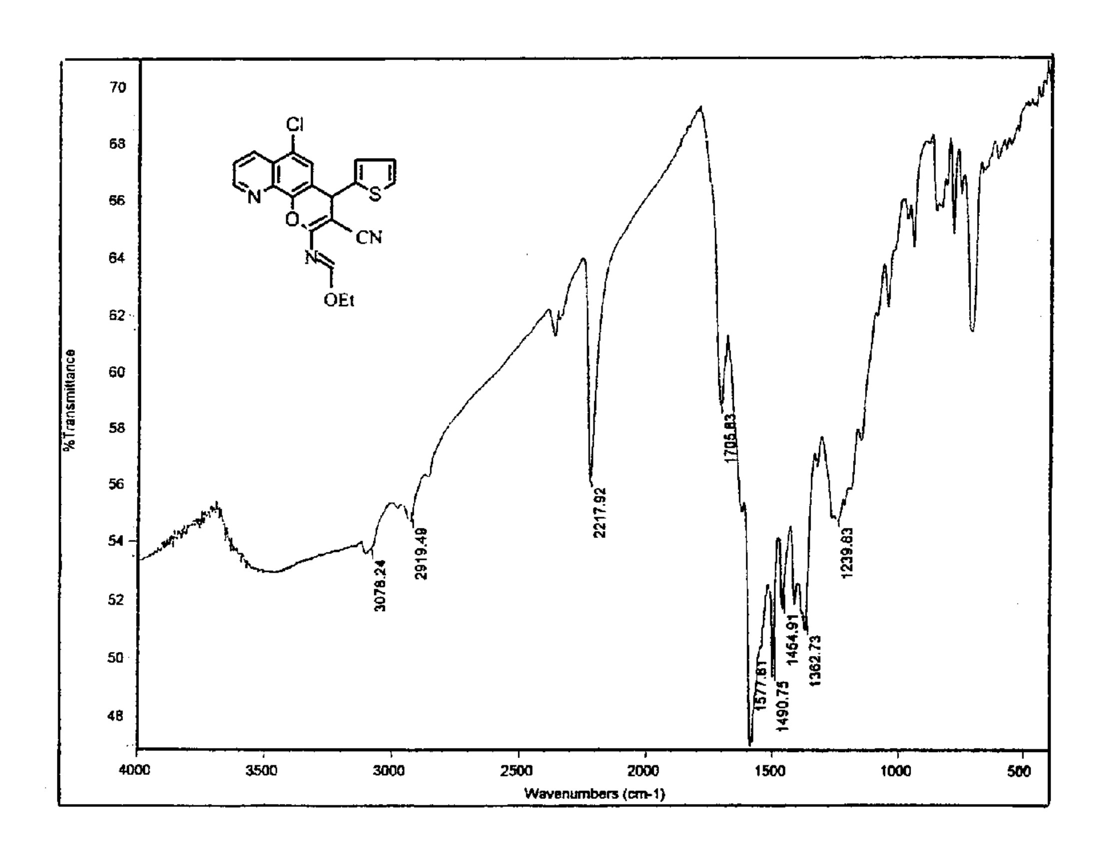


Fig.(27): 3-Cyano-6-chloro-2-(ethoxymethylenamino)-4-thienyl-4H-pyrano-[3,2-h]quinoline **(223_e)**.

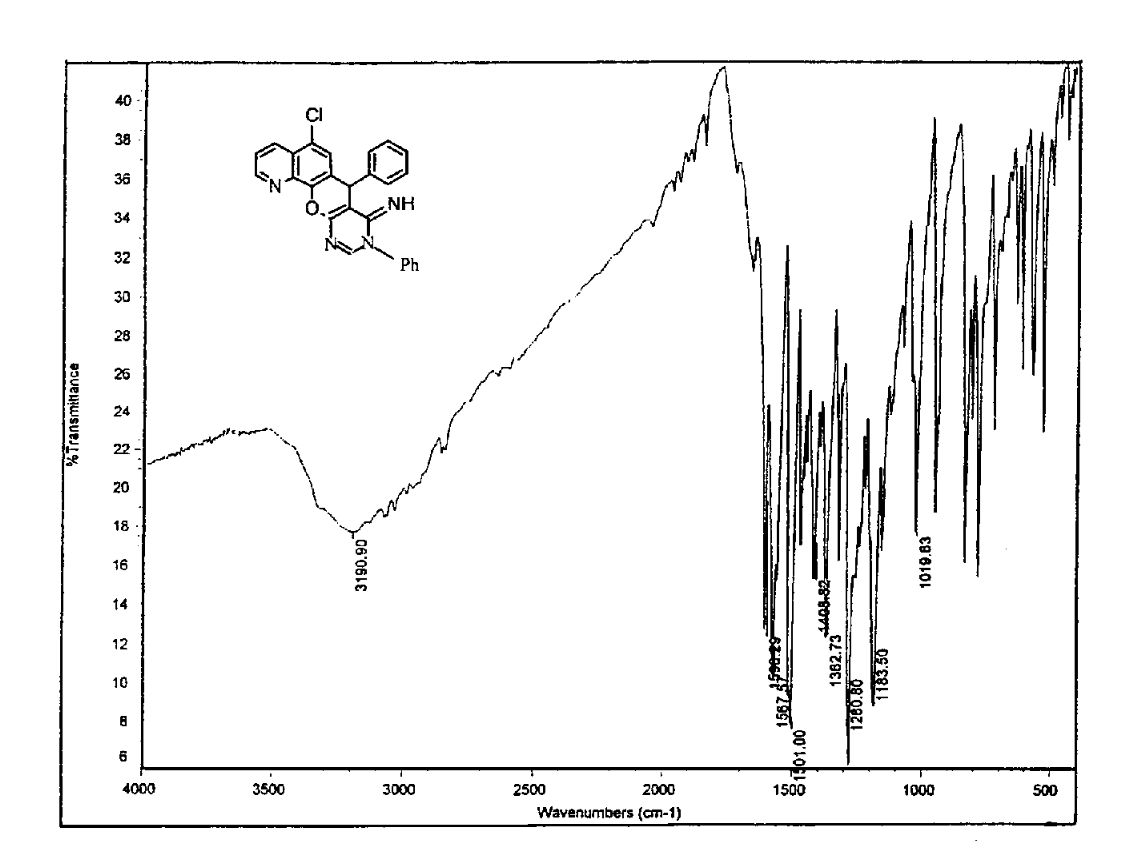
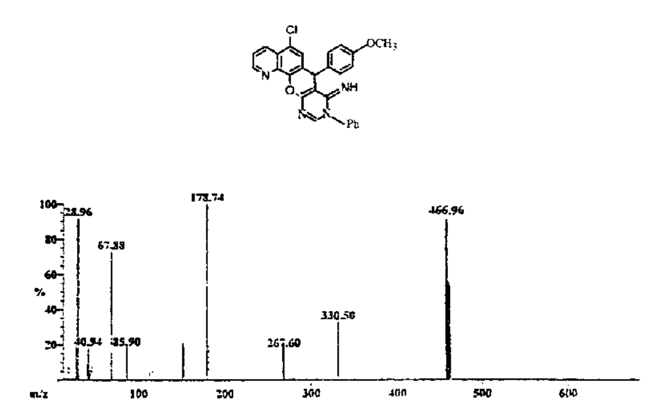


Fig.(28): 5-Chloro-7,9-diphenyl-8-imino-7H-pyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**224**$_a$).



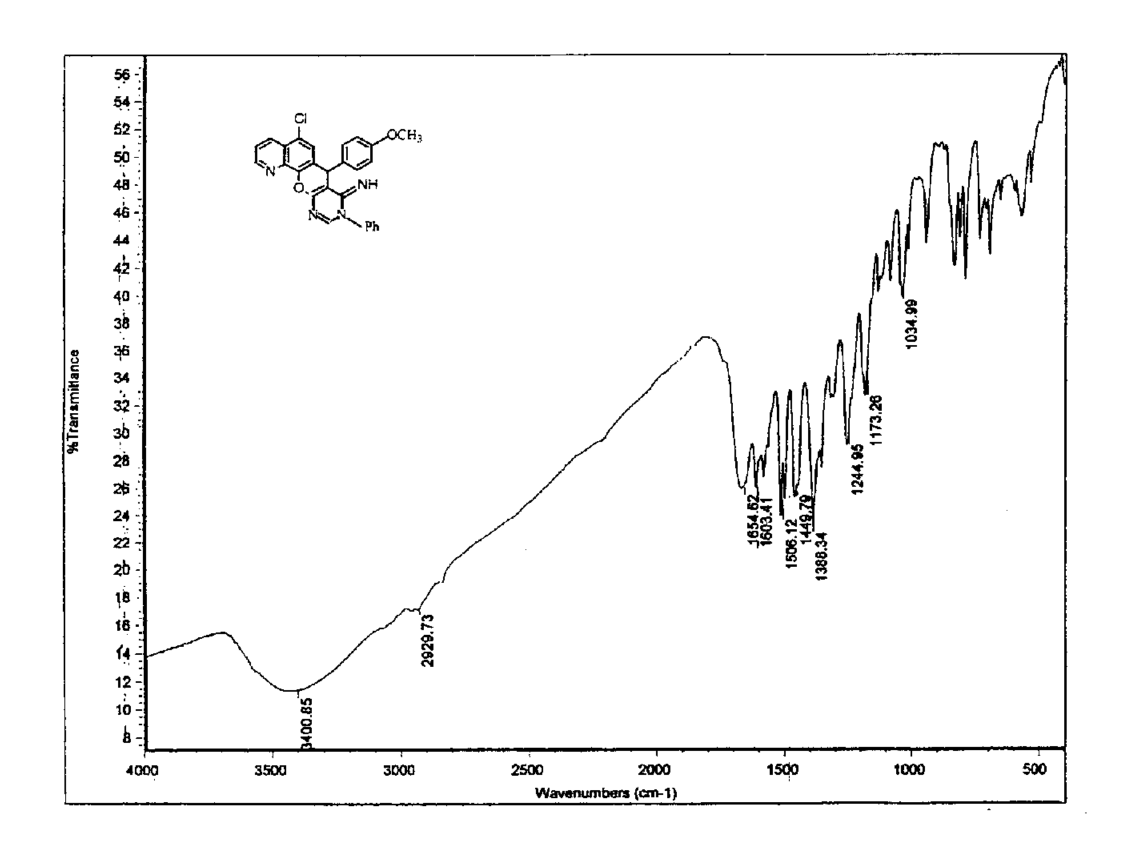


Fig.(29): 5-Chloro-8-imino-7-(4-methoxy)phenyl-7H-9-phenylpyrimido-[4',5':6,5]pyrano[3,2-h]quinoline **(224_b)**.

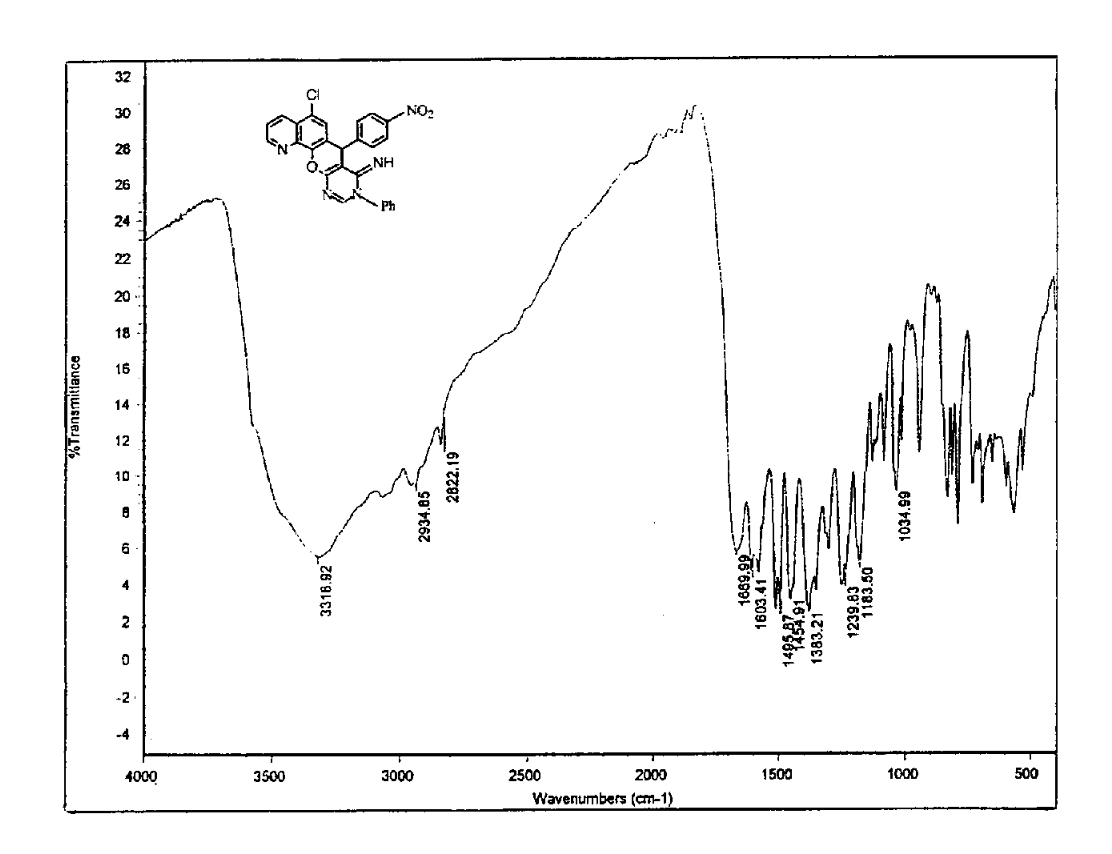


Fig.(30): 5-Chloro-8-imino-7-(4-nitro)phenyl-7H-9-phenylpyrimido-[4',5':6,5]pyrano[3,2-h]quinoline **(224$_c$)**.

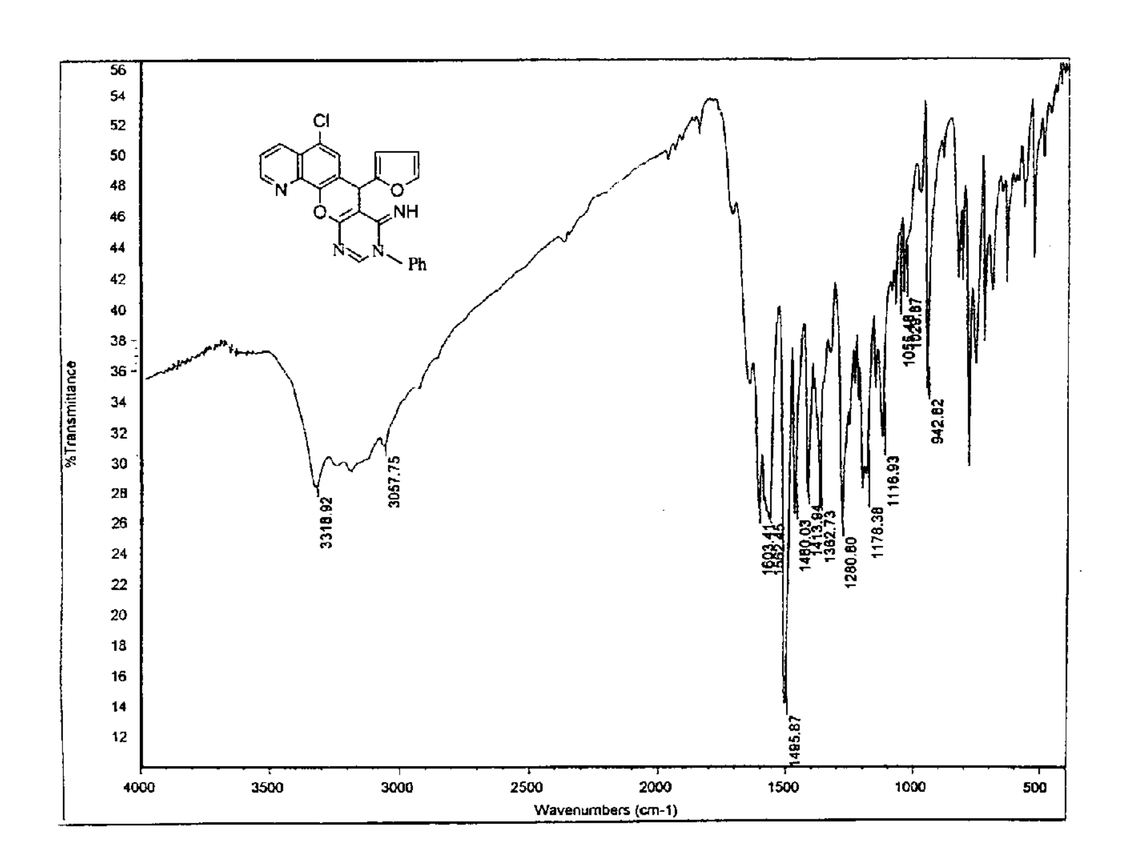


Fig.(31): 5-Chloro-8-imino-7-furyl-7H-9-phenylpyrimido[4',5':6,5]pyrano-[3,2-h]quinoline **(224_d)**.

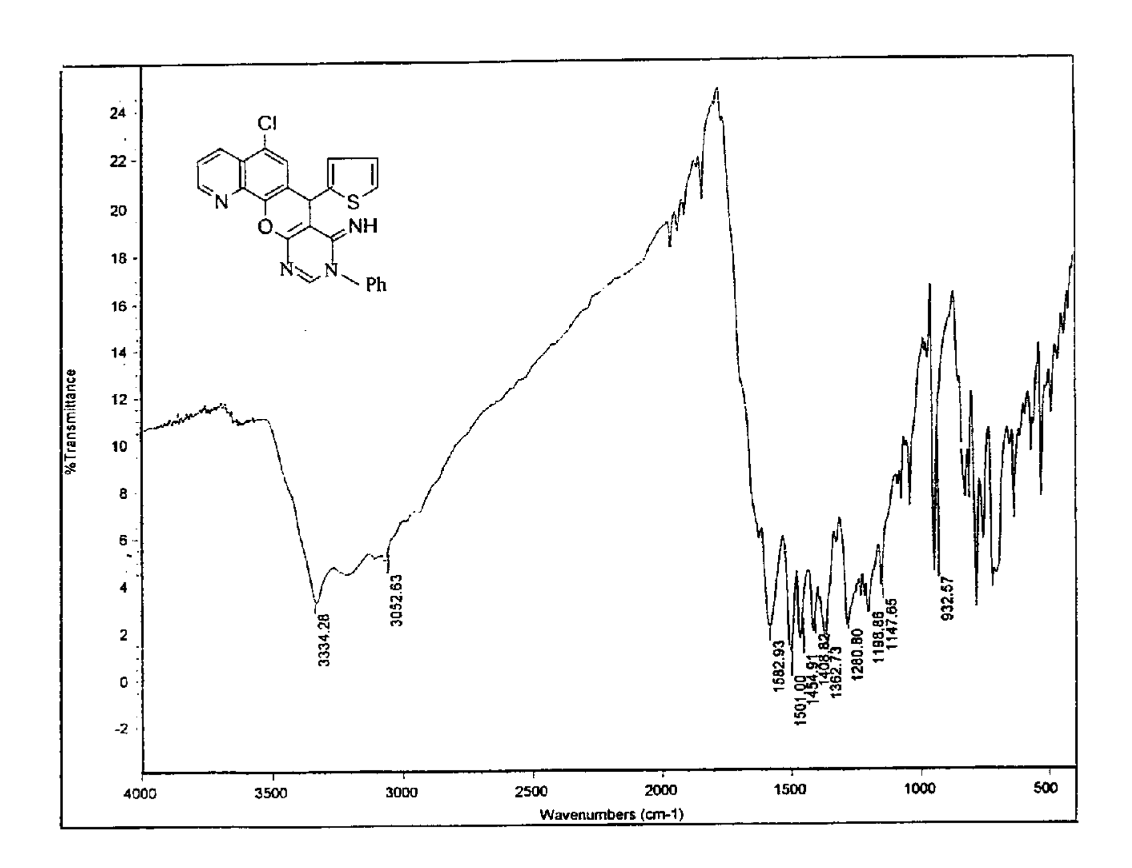


Fig.(32): 5-Chloro-8-imino-7-thienyl-7H-9-phenylpyrimido[4',5':6,5]pyrano-[3,2-h]quinoline (**224_e**).

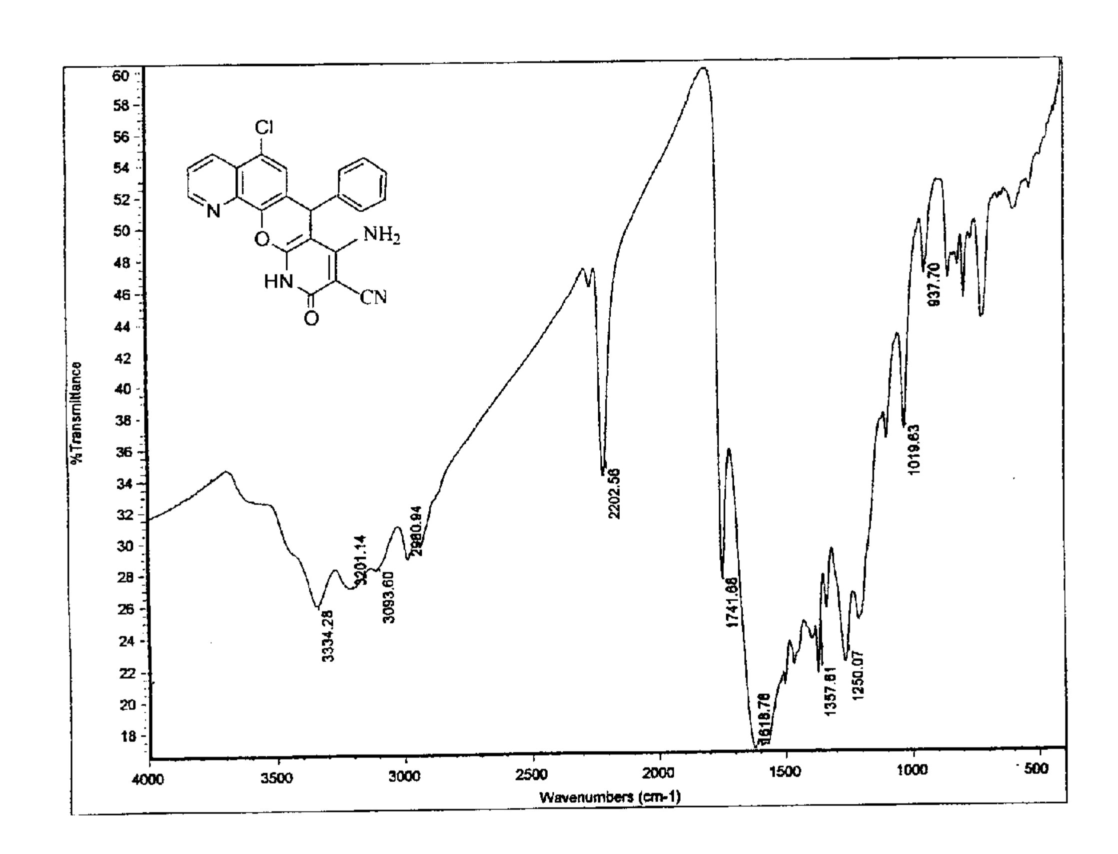
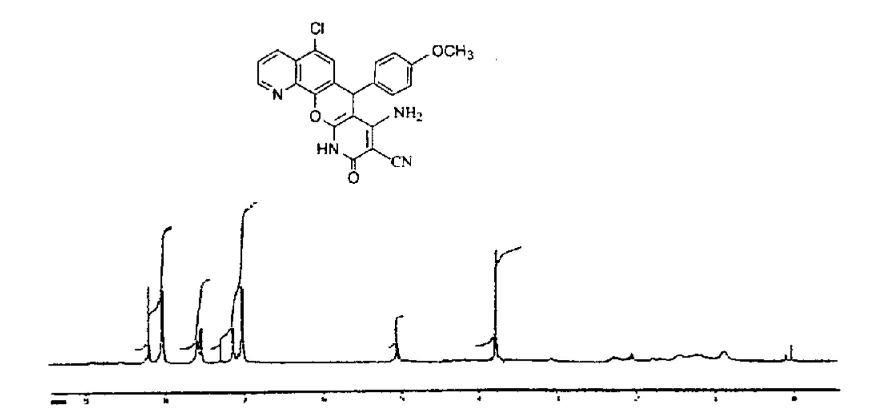


Fig.(33): 8-Amino-5-chloro-9-cyano-7-phenyl-7H-10-oxo-10,11-dihydropyrido-[2',3':6,5]pyrano[3,2-h]quinoline **(225_a)**.



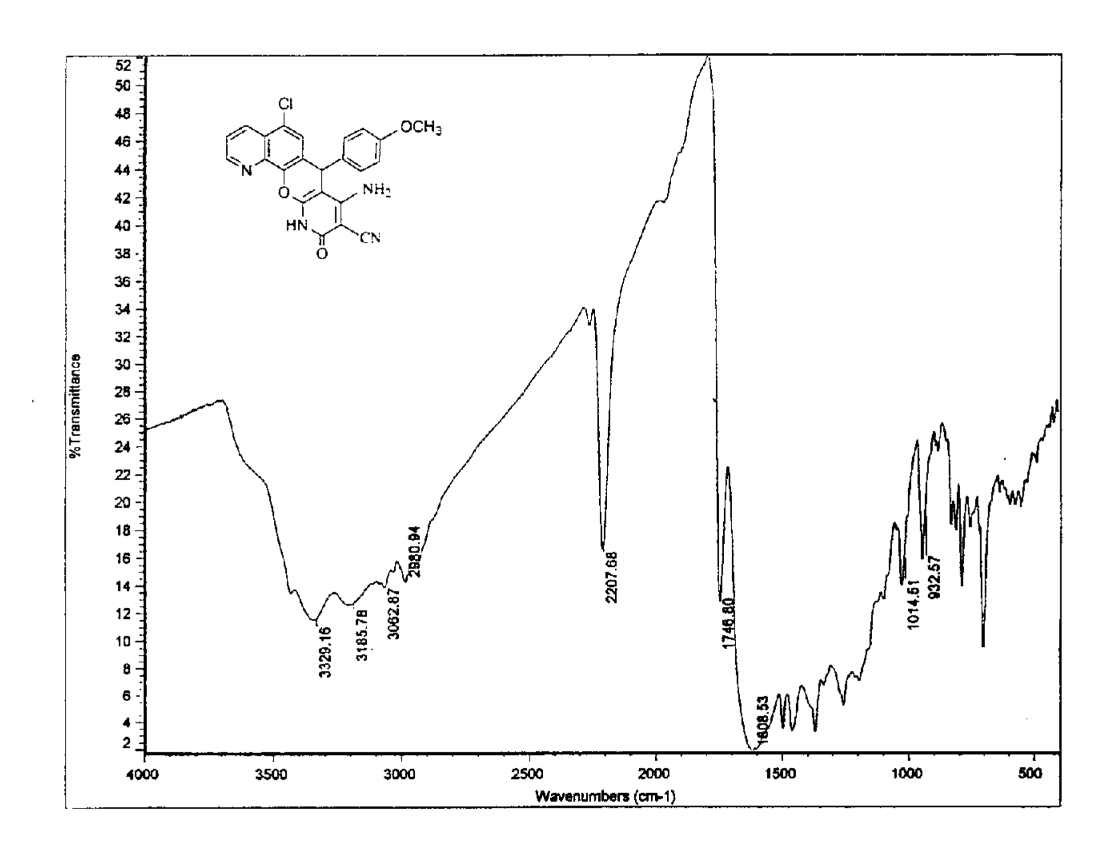


Fig.(34): 8-Amino-5-chloro-9-cyano-7-(4-methoxy)phenyl-7H-10-oxo-10,11-dihydropyrido[2',3':6,5]pyrano[3,2-h]quinoline **(225$_b$)**.

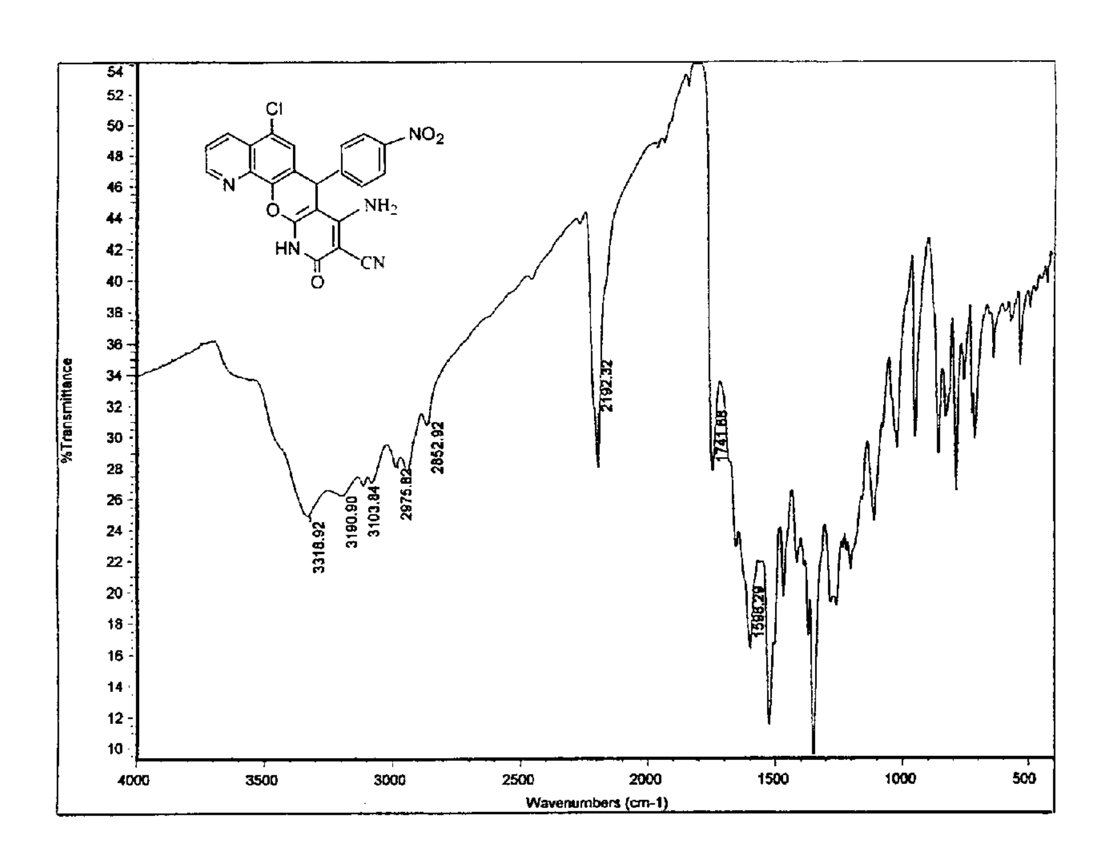


Fig.(35): 8-Amino-5-chloro-9-cyano-7-(4-nitro)phenyl-7H-10-oxo-10,11-dihydropyrido[2',3':6,5]pyrano[3,2-h]quinoline **(225_c)**.

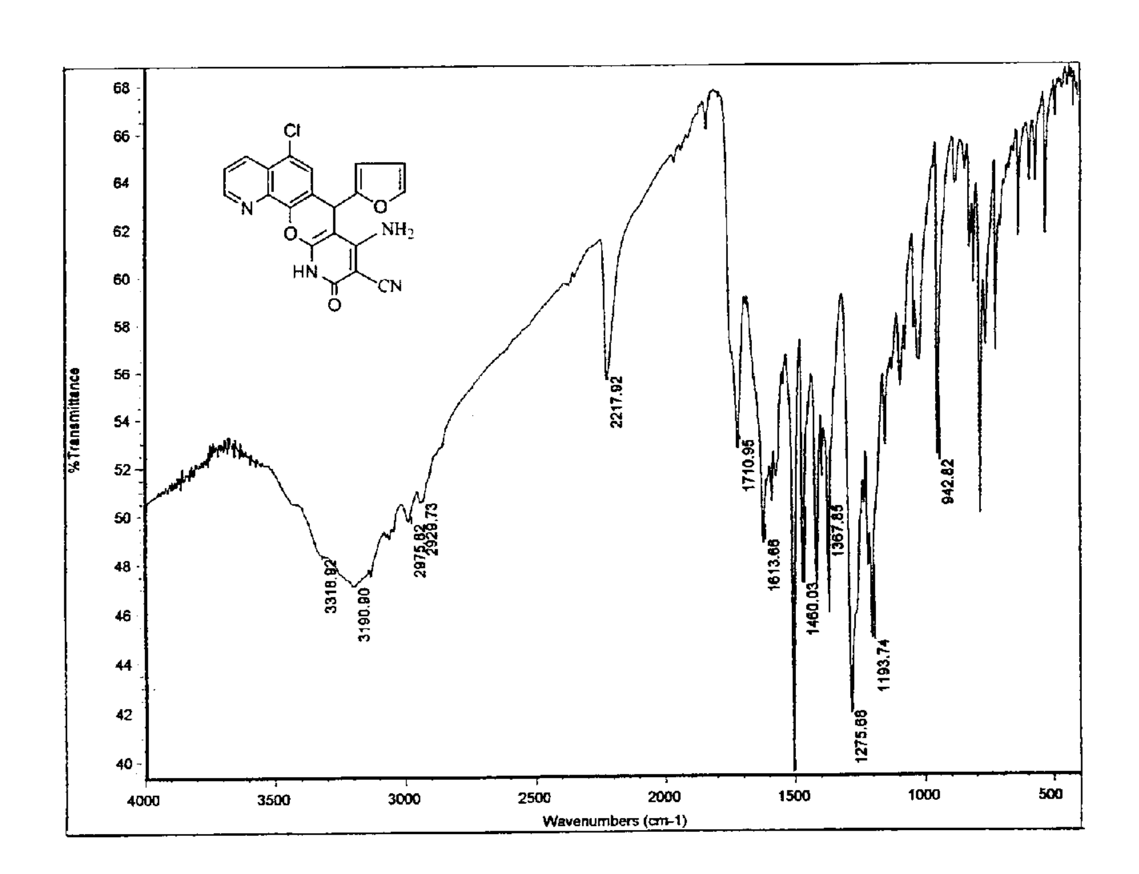


Fig.(36): 8-Amino-5-chloro-9-cyano-7-furyl-7H-10-oxo-10,11-dihydropyrido [2',3':6,5]pyrano[3,2-h]quinoline **(225_d)**.

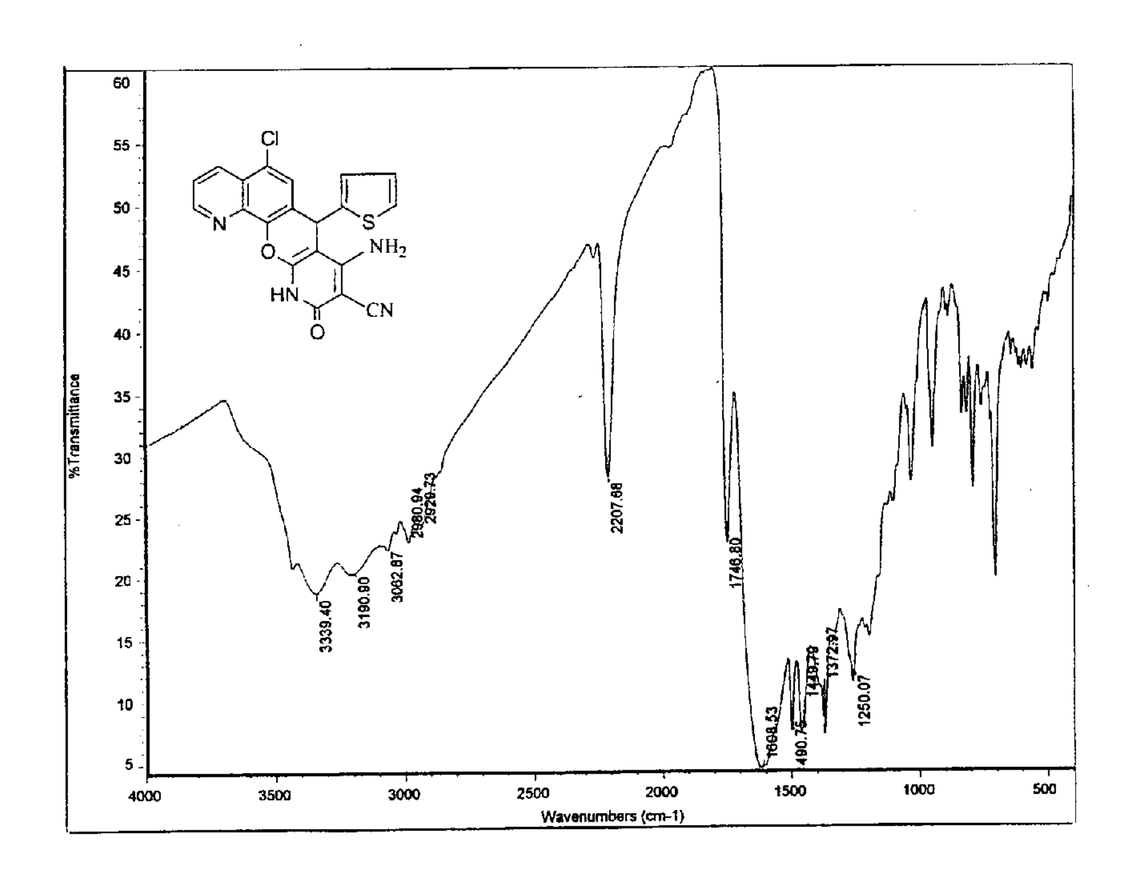


Fig.(37): 8-Amino-5-chloro-9-cyano-7-thienyl-7H-10-oxo-10,11-dihydropyrido-[2',3':6,5]pyrano[3,2-h]quinoline **(225_e)**.

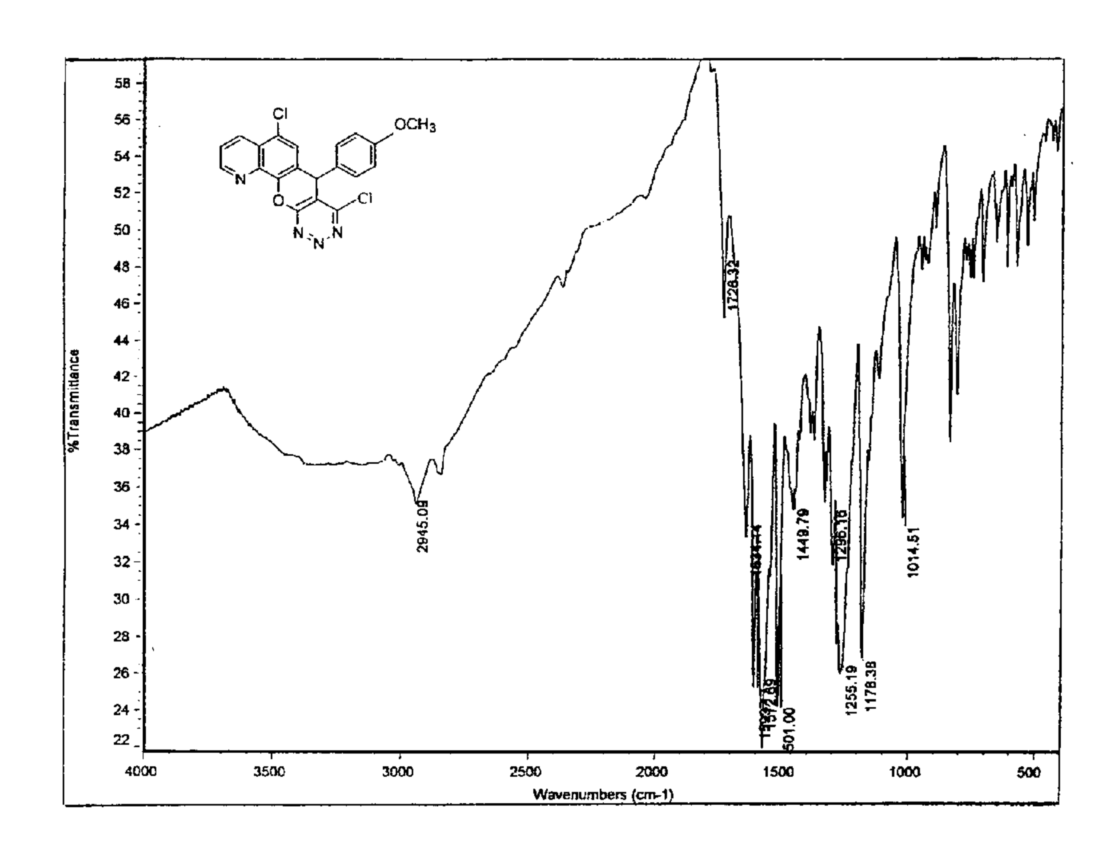


Fig.(38): 4,7-Dichloro-5-(4-methoxy)phenyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline **(226$_b$)**.

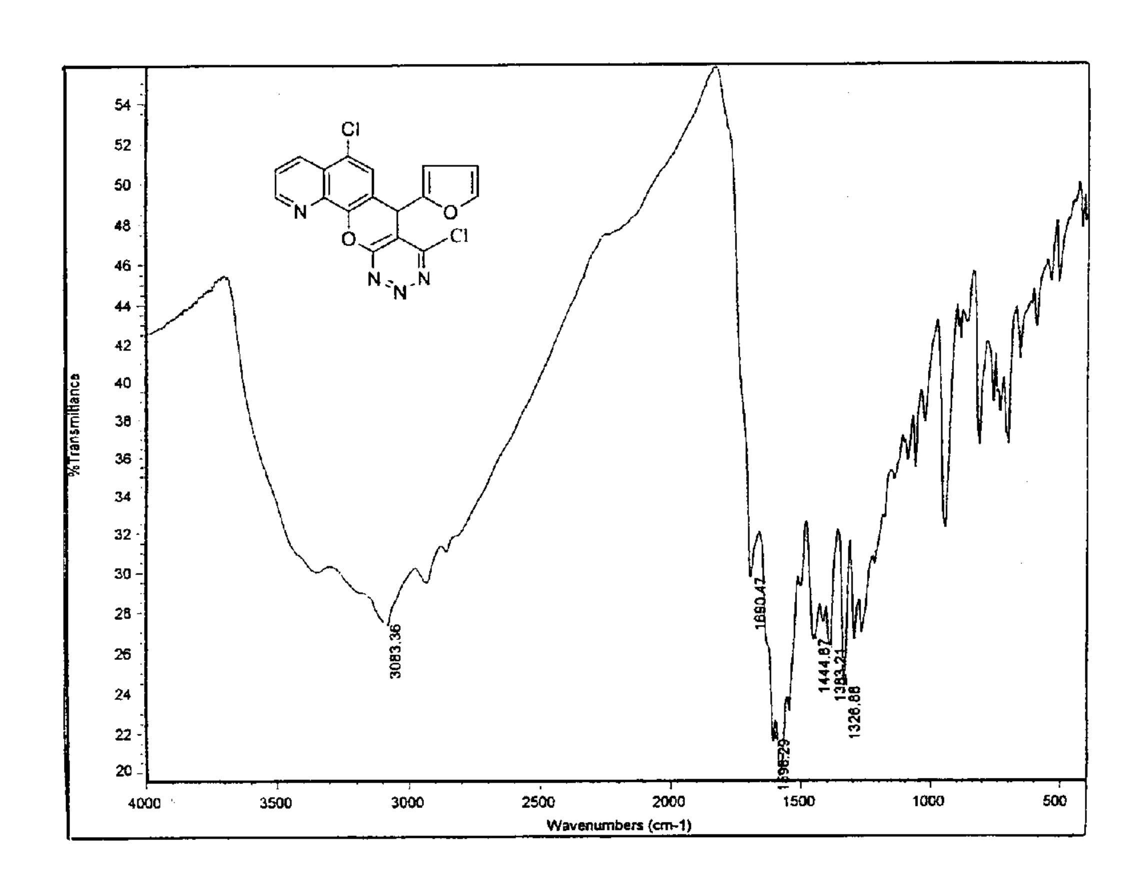


Fig.(39): 4,7-Dichloro-5-furyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline **(226$_d$)**.

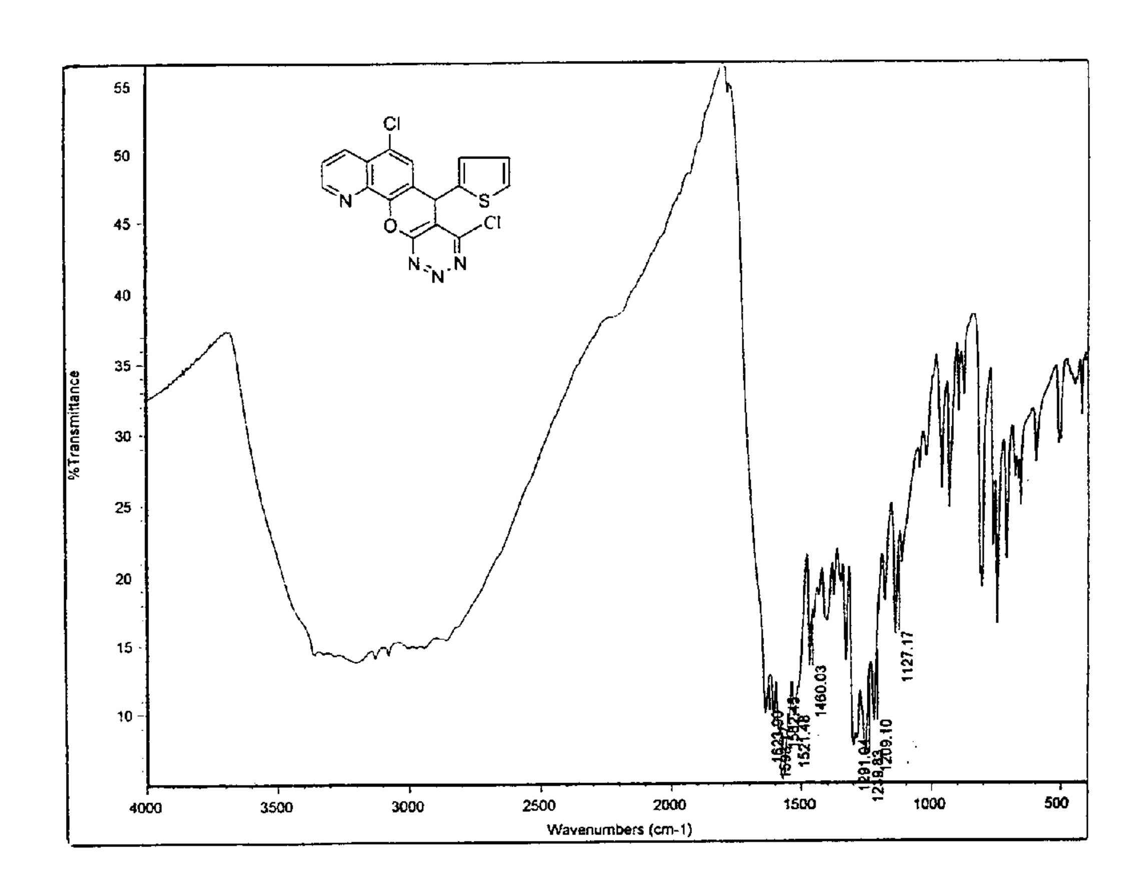
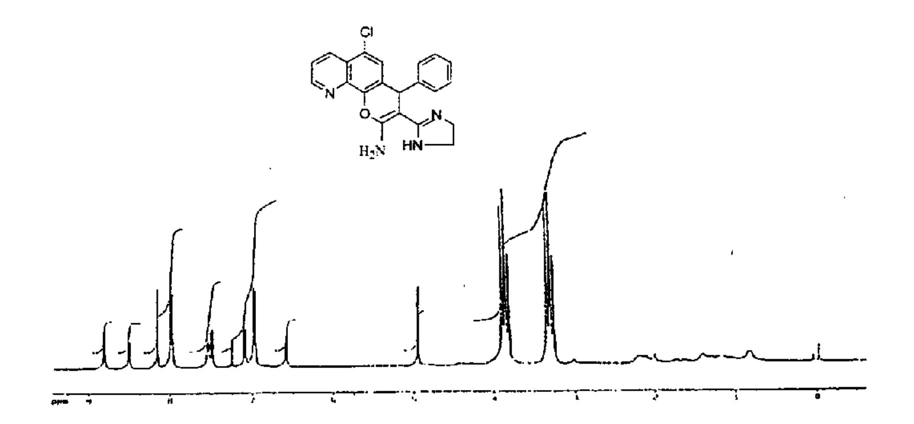


Fig.(40): 4,7-Dichloro-5-thienyl-5H-[1,2,3]triazino[5',4':5,6]pyrano-[3,2-h]quinoline **(226$_e$)**



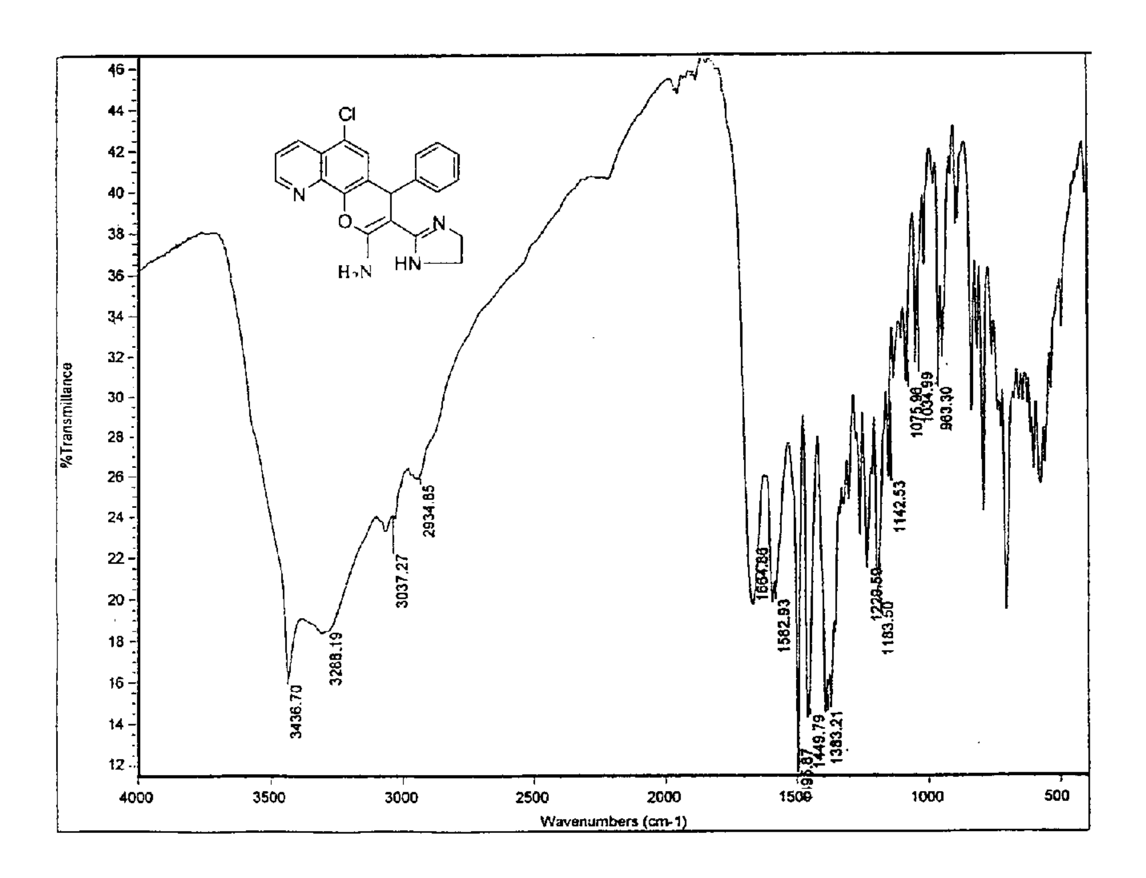


Fig.(41): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-phenyl-4H-pyrano-[3,2-h]quinoline **(227_a)**.

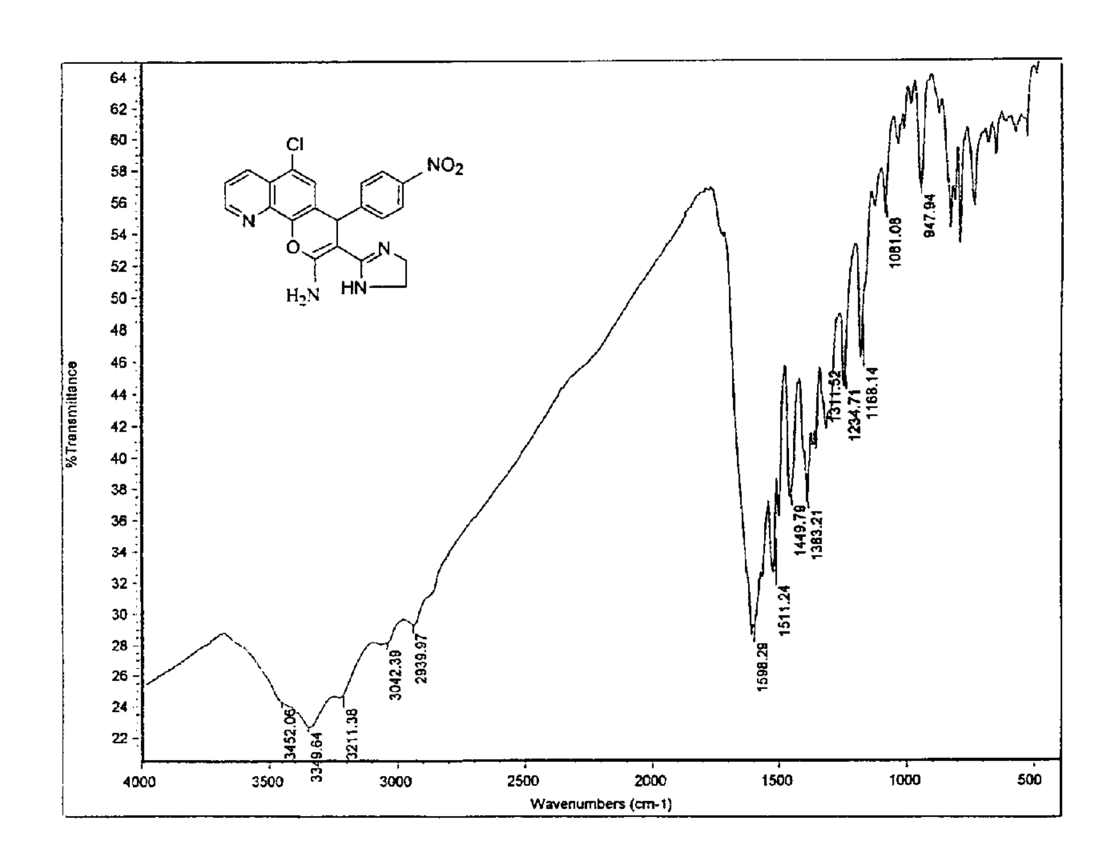


Fig.(42): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano[3,2-h]quinoline (**227_c**).

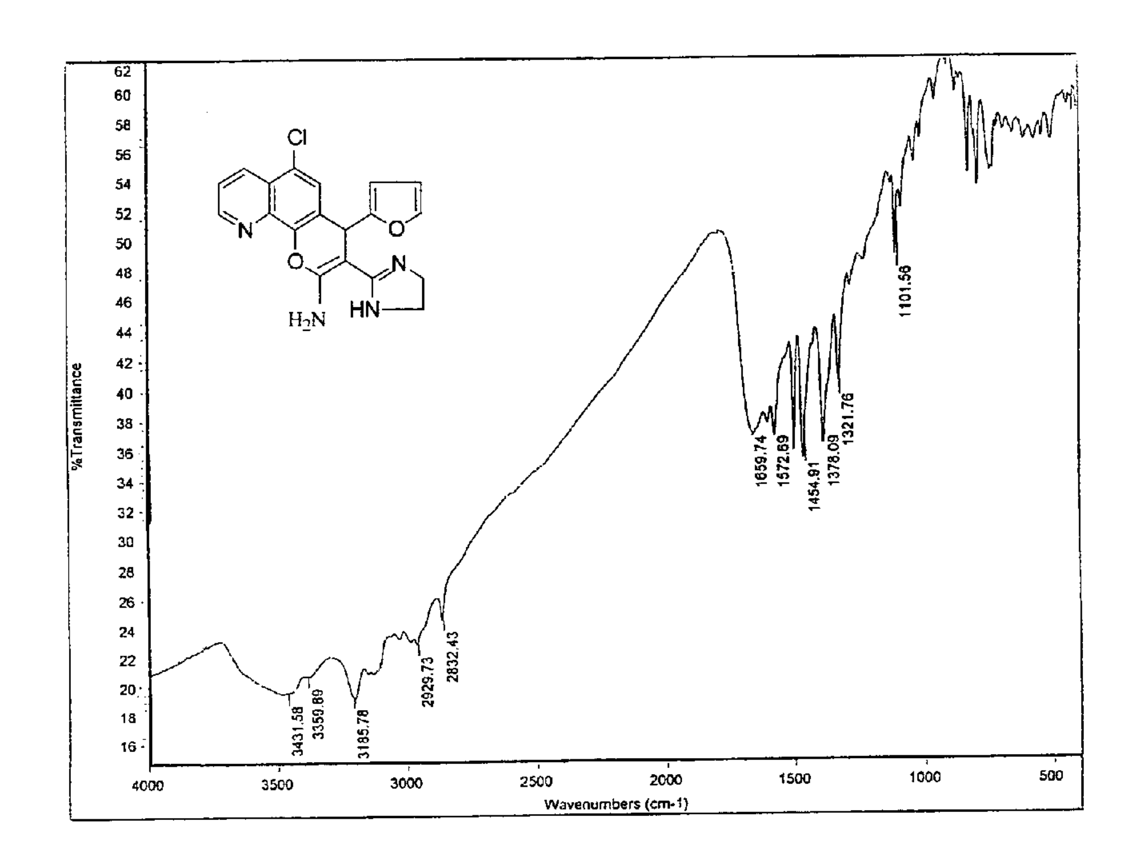


Fig.(43): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-furyl-4H-pyrano-[3,2-h]quinoline **(227_d)**.

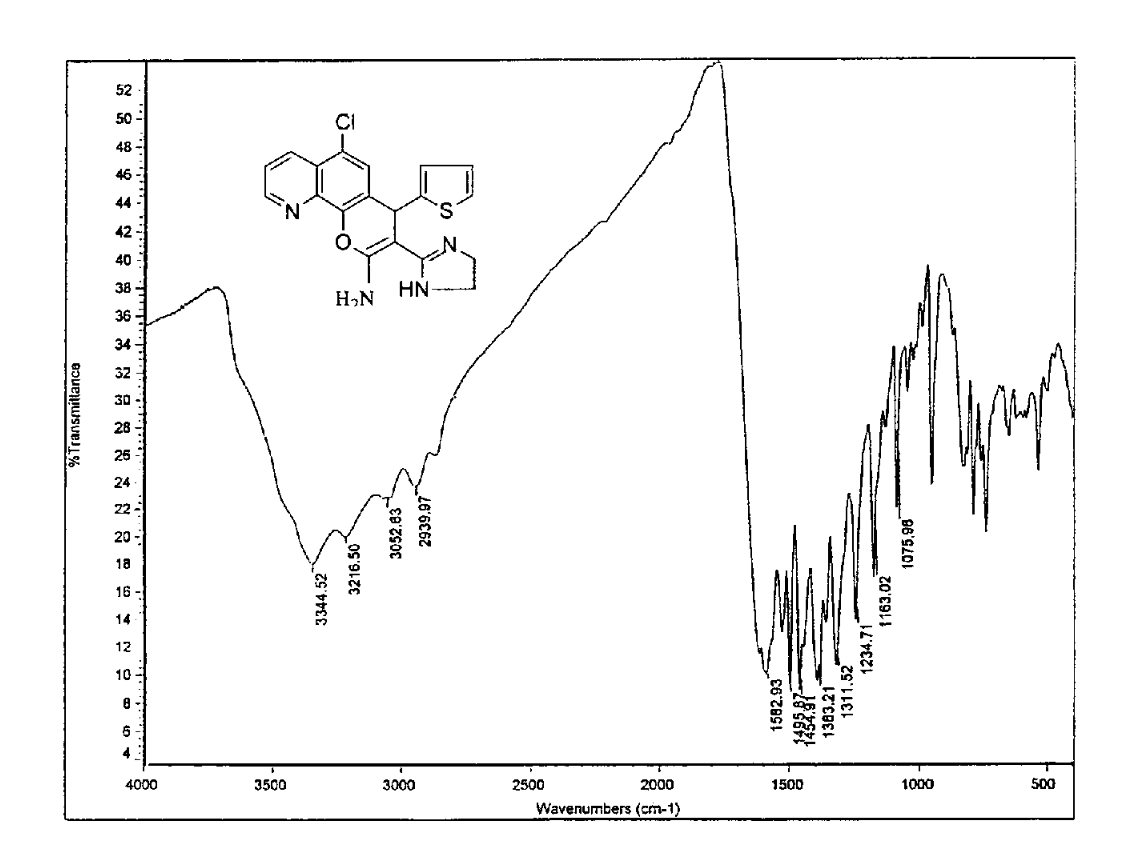


Fig.(44): 2-Amino-3-(4',5'-dihydro-1H-imidazol-2-yl)-4-thienyl-4H-pyrano-[3,2-h]quinoline **(227_e)**.

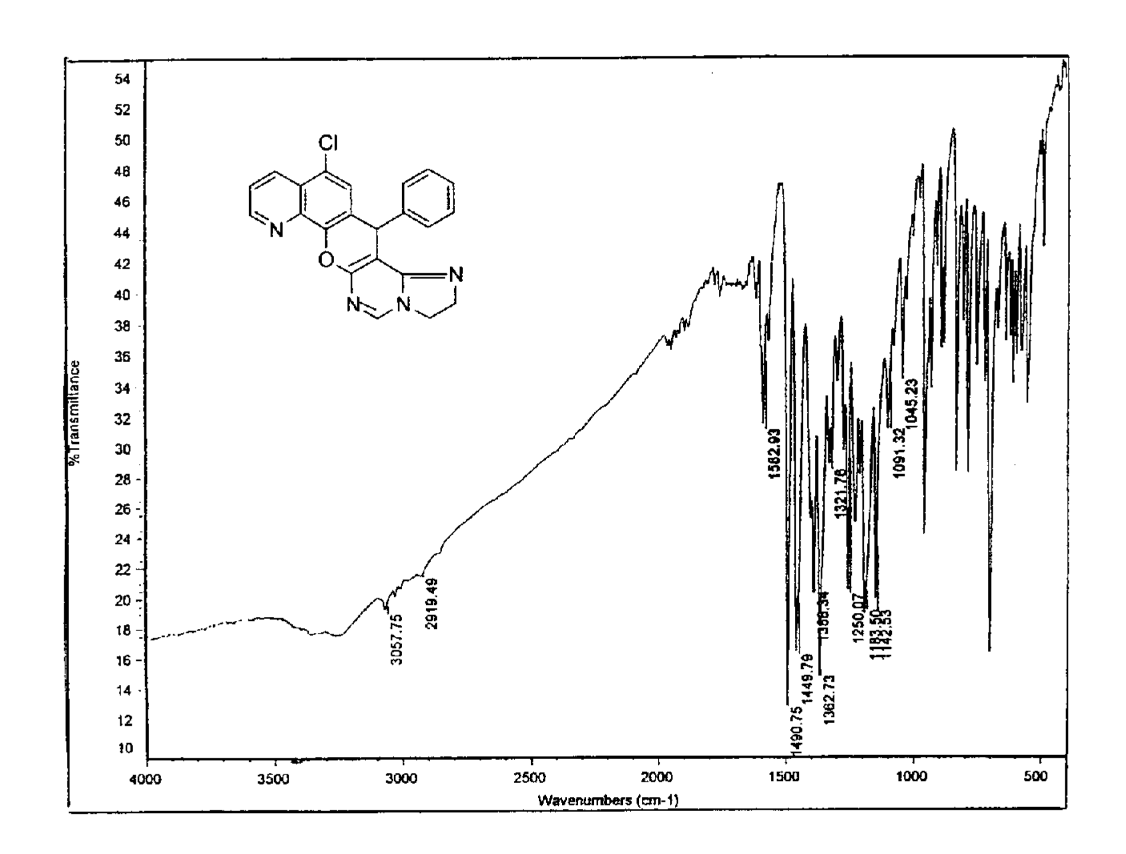


Fig.(45): 12-Chloro-14-phenyl-1,3,14-trihydroimidazo[1,2-c]pyrimido [4',5':6,5]pyrano[3,2-h]quinoline **(228_a)**.

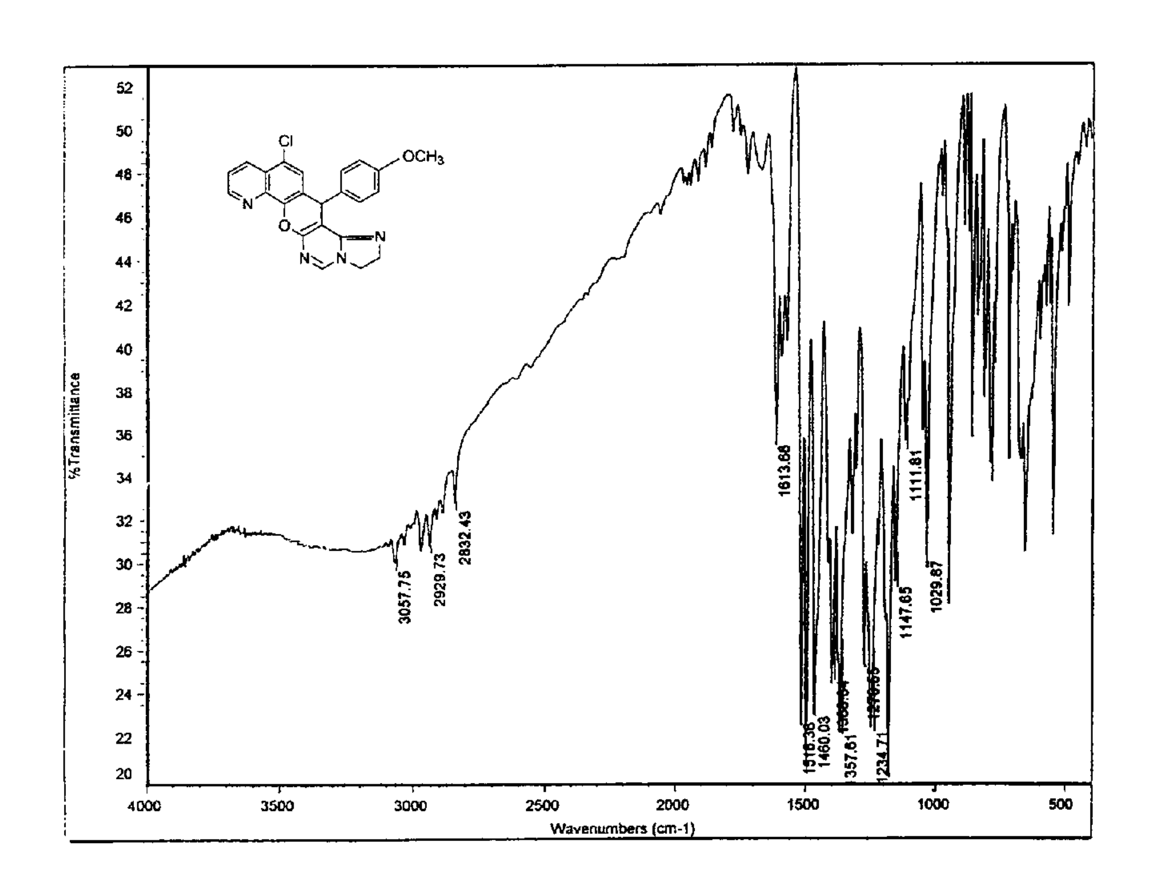


Fig.(46): 12-Chloro-14-(4-methoxy)phenyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(228$_b$)**.

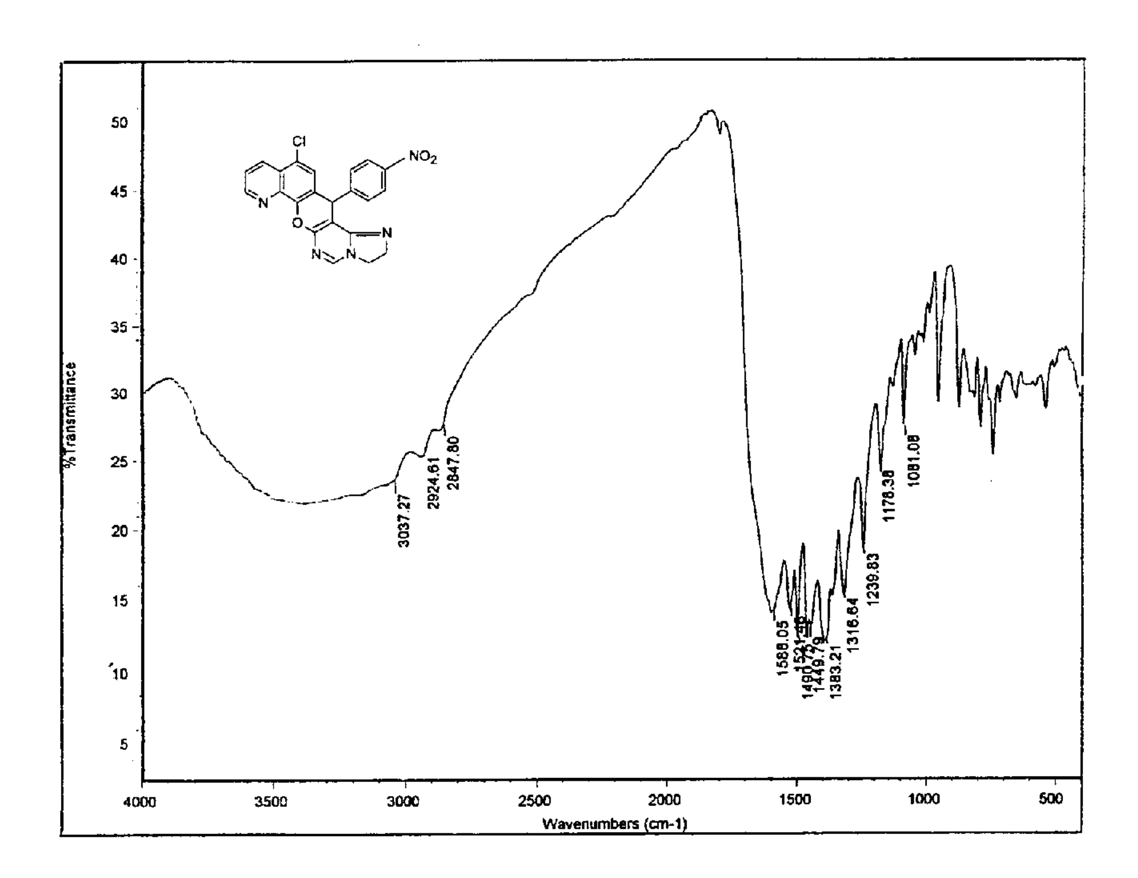


Fig.(47): 12-Chloro-14-(4-nitro)phenyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(228_c)**.

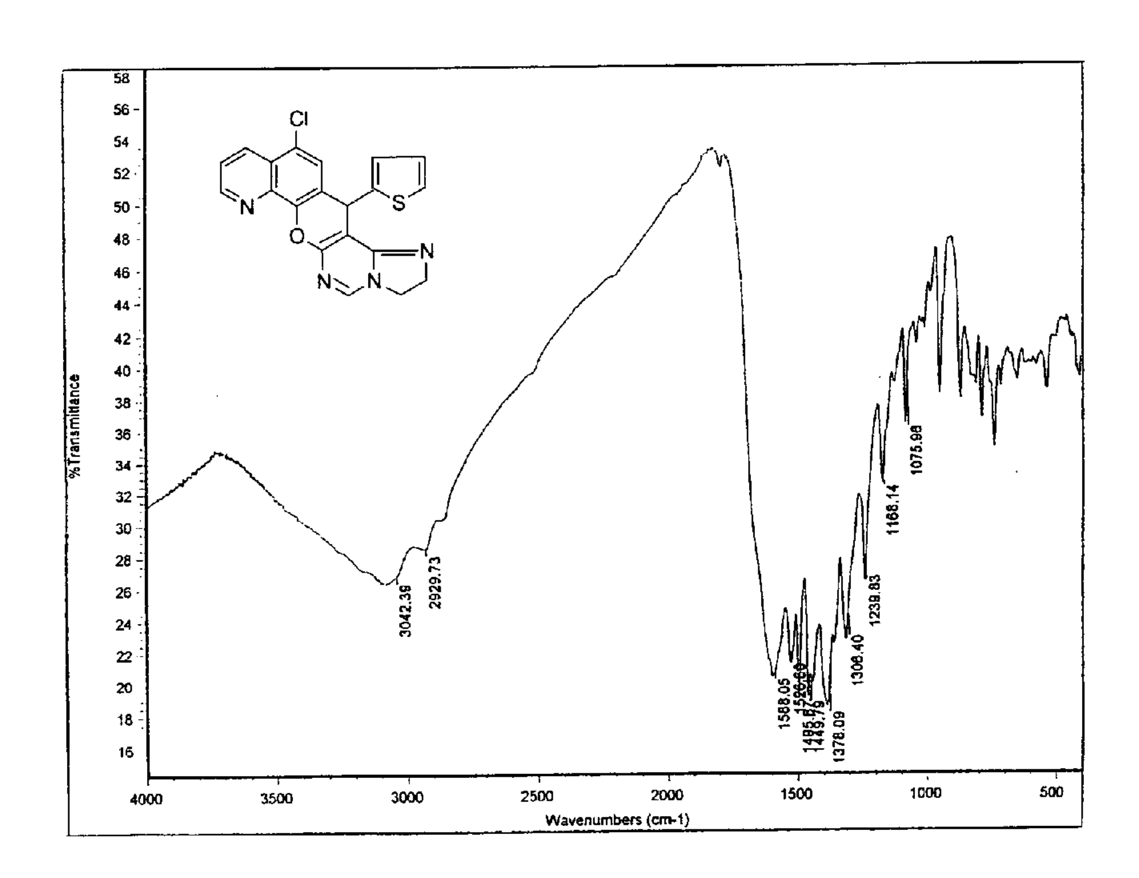


Fig.(48): 12-Chloro-14-thienyl-1,3,14-trihydroimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**228_e**).

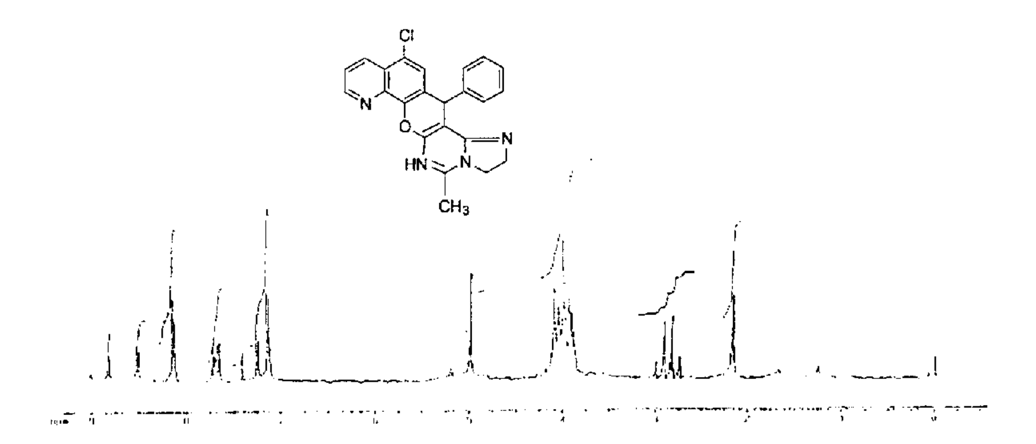


Fig.(49): 12-Chloro-5-methyl-14-phenyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(229_a)**.

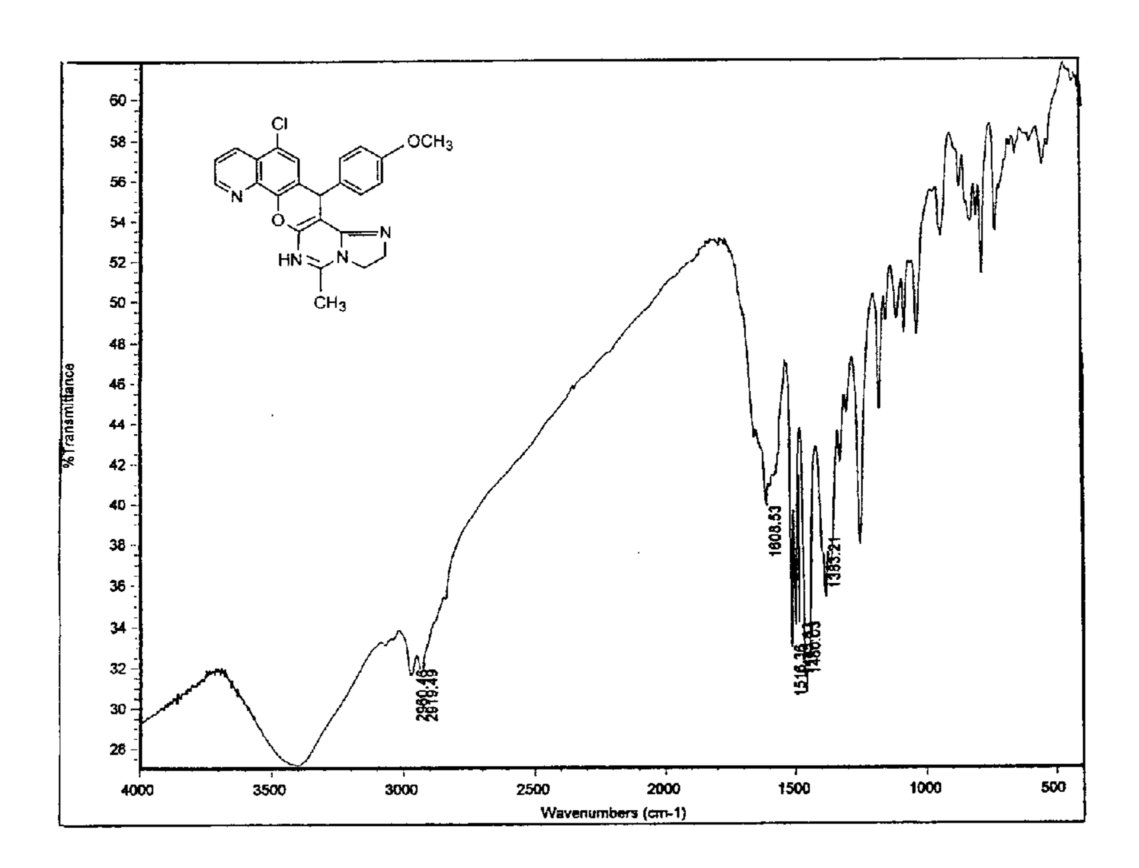


Fig.(50): 12-Chloro-5-methyl-14-(4-methoxy)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(229_b)**.

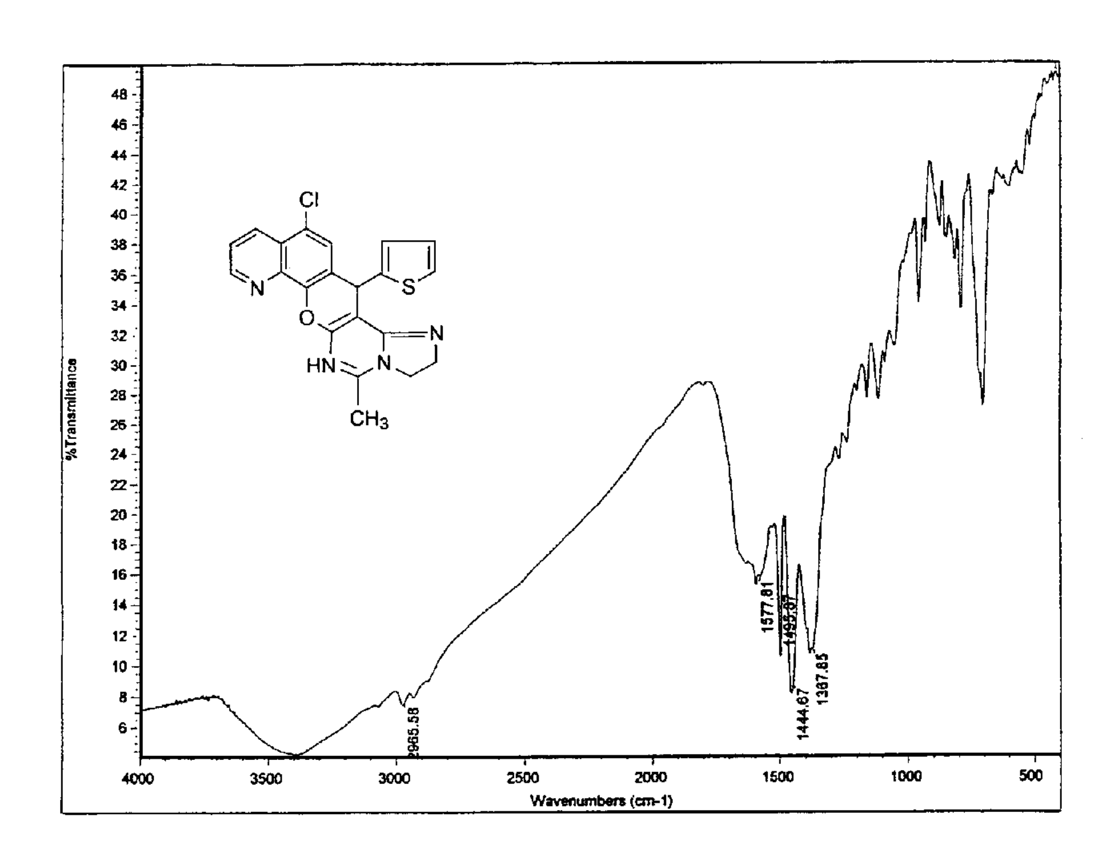
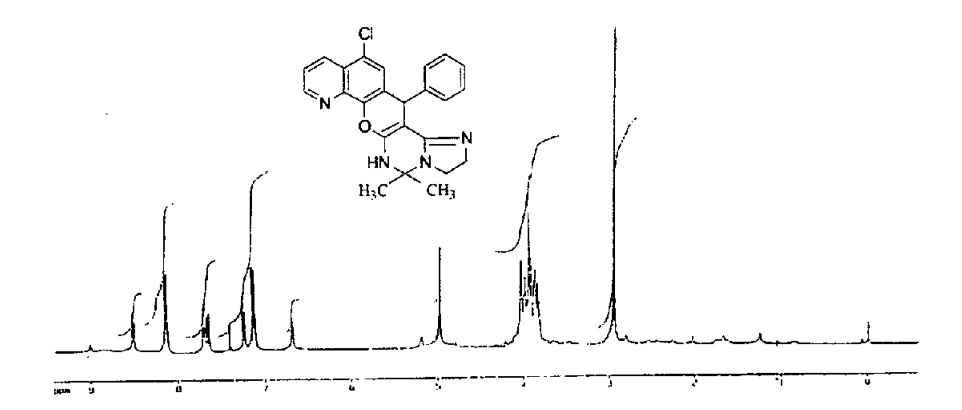


Fig.(51): 12-Chloro-5-methyl-14-thienyl-2,3,5,6,14- pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(229$_e$)**.



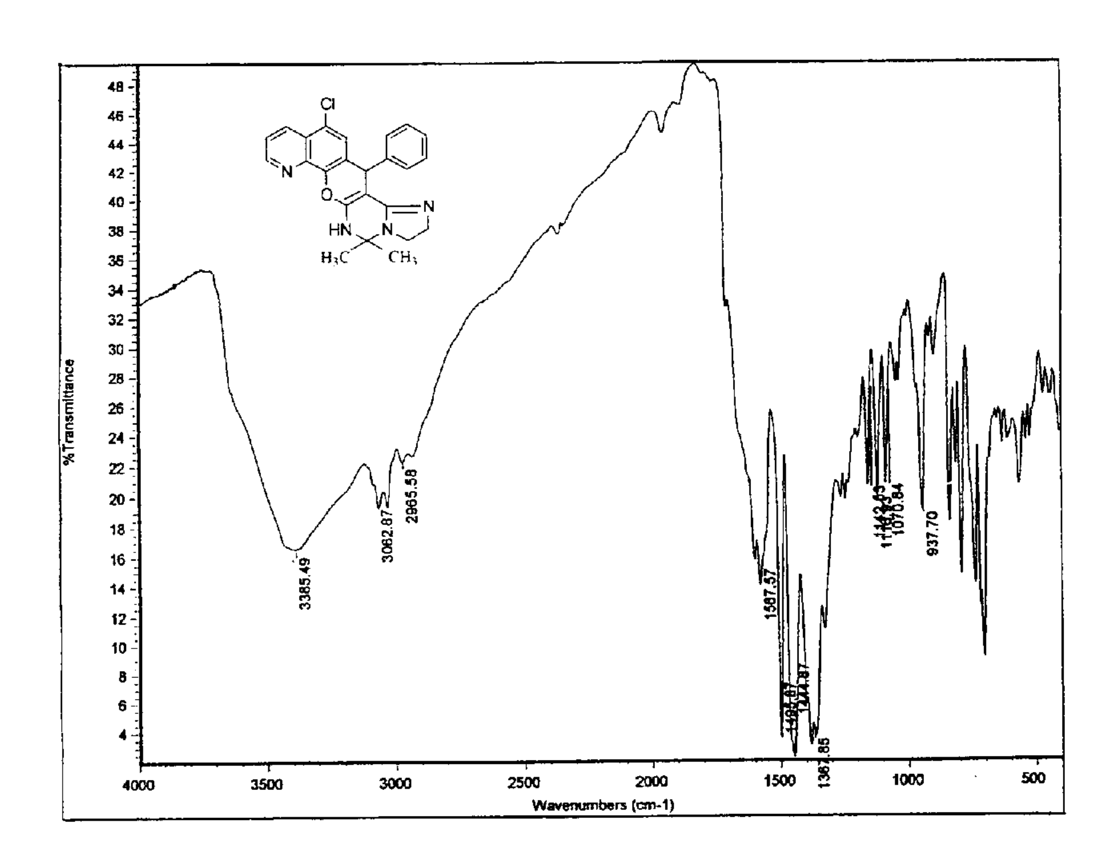


Fig.(52): 12-Chloro-5,5-dimethyl-14-phenyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(230_a)**.

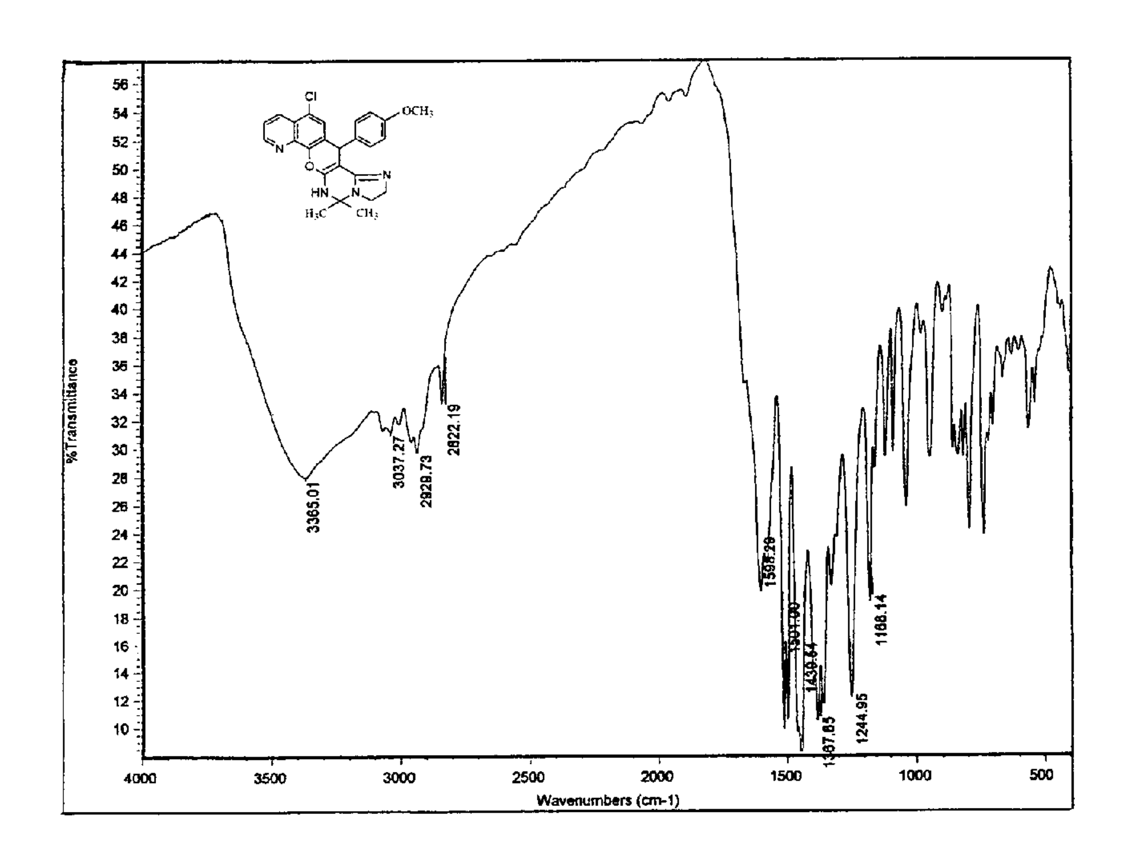


Fig.(53): 12-Chloro-5,5-dimethyl-14-(4-methoxy)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(230_b)**.

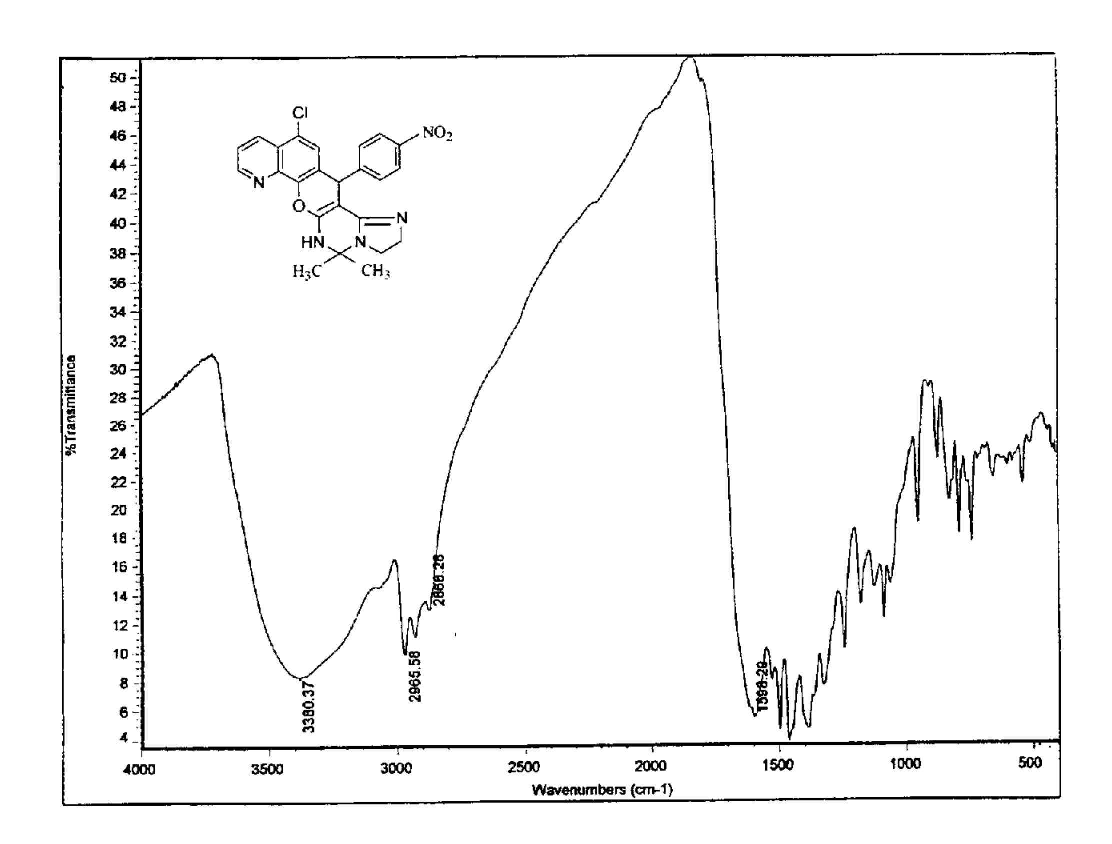


Fig.(54): 12-Chloro-5,5-dimethyl-14-(4-nitro)phenyl-2,3,5,6,14-pentahydroimidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(230$_c$)**.

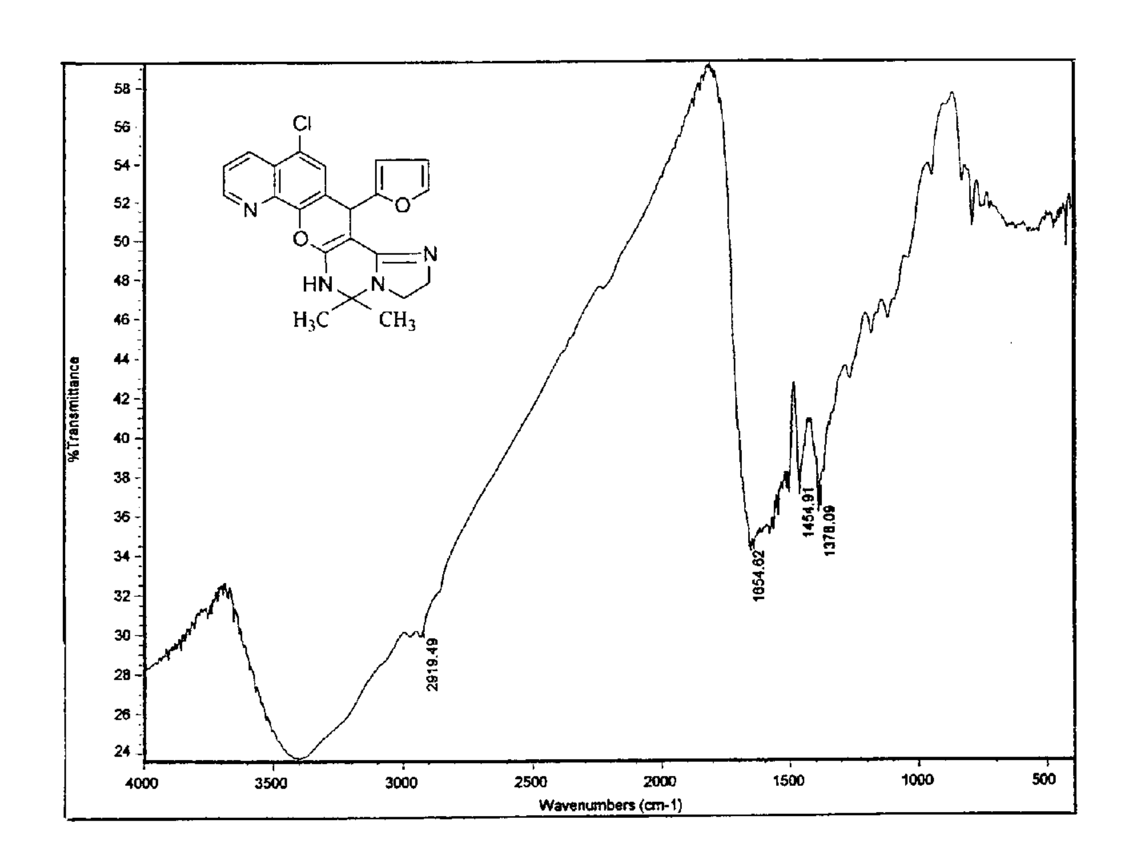


Fig.(55): 12-Chloro-5,5-dimethyl-14-furyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**230$_d$**).

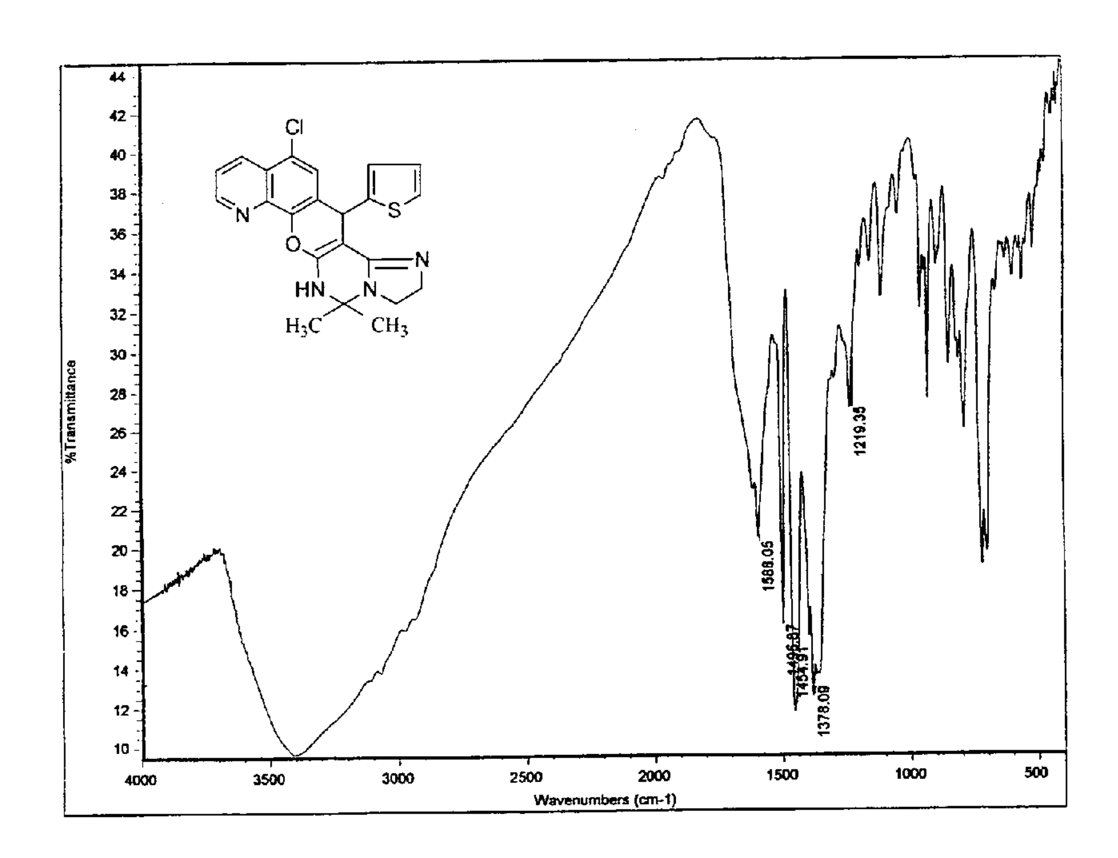


Fig.(56): 12-Chloro-5,5-dimethyl-14-thienyl-2,3,5,6,14-pentahydroimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(230$_e$)**.

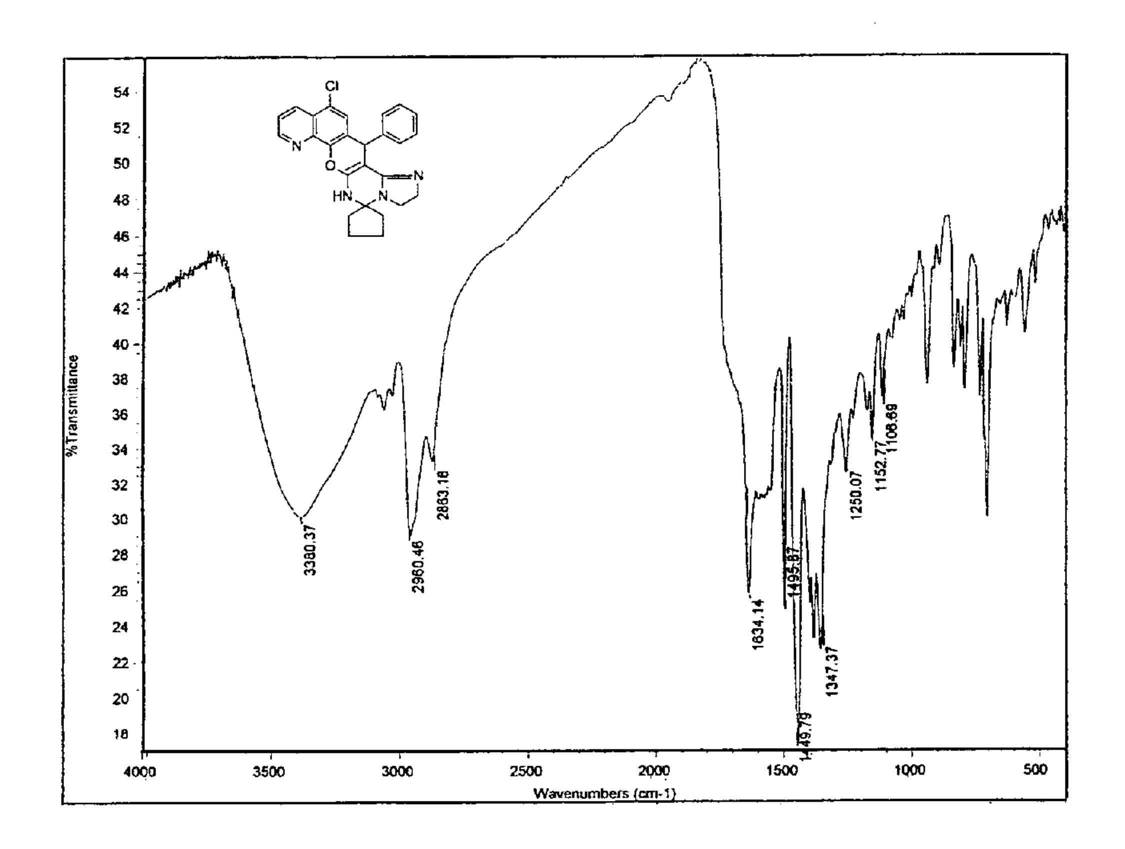


Fig.(57): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-spiro(1'-cycloheptane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(231a)**.

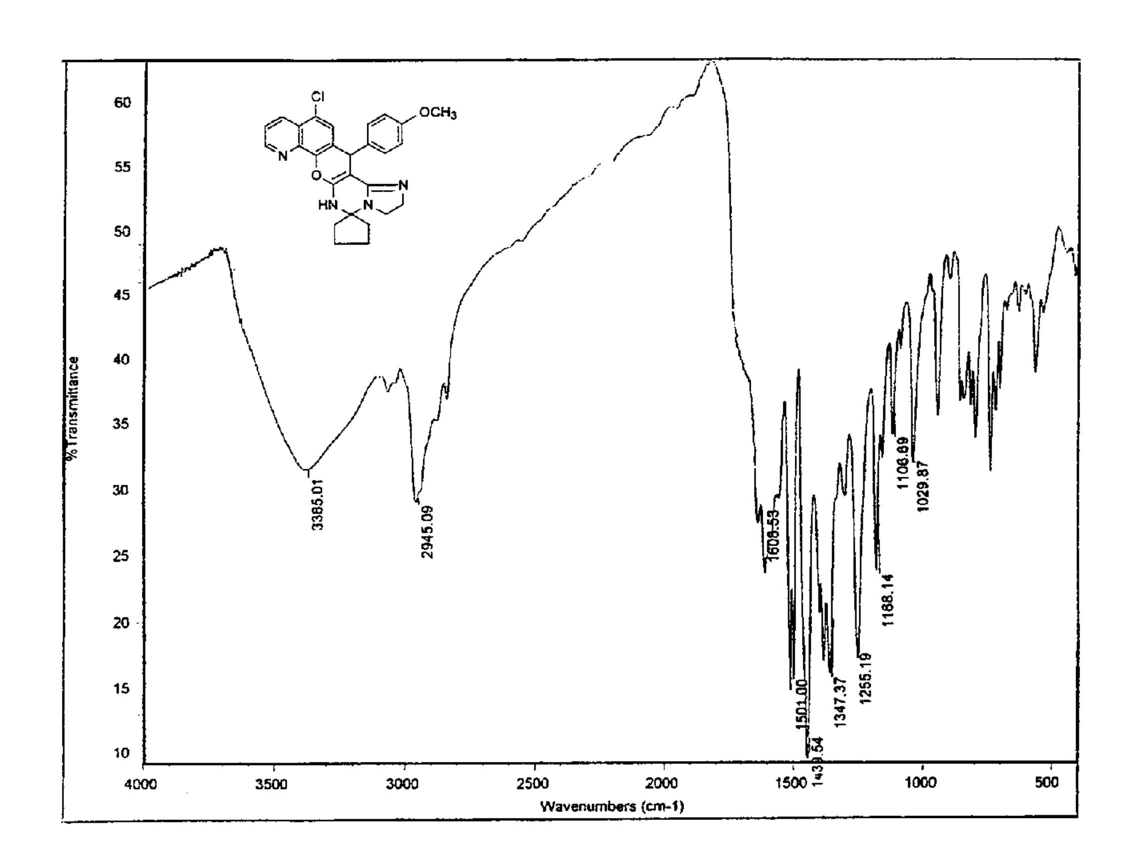
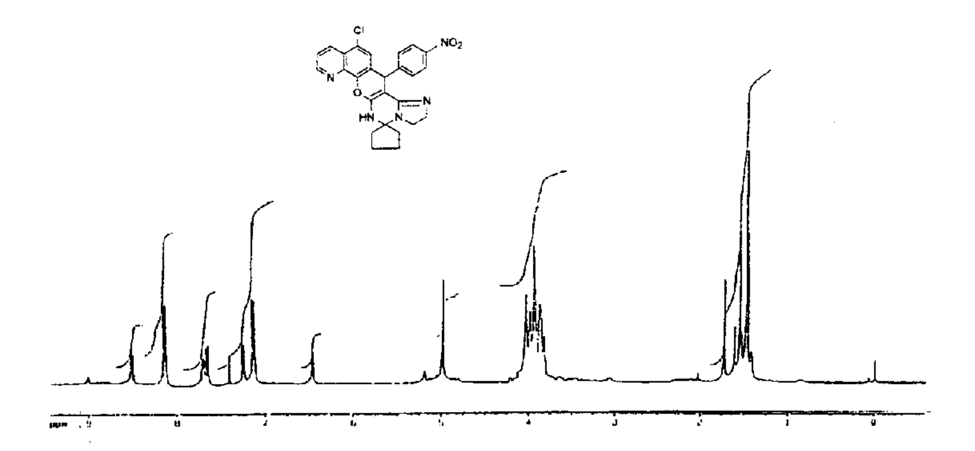


Fig.(58): 12-Chloro-14-(4-mehoxy)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclopentane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(231_b)**.



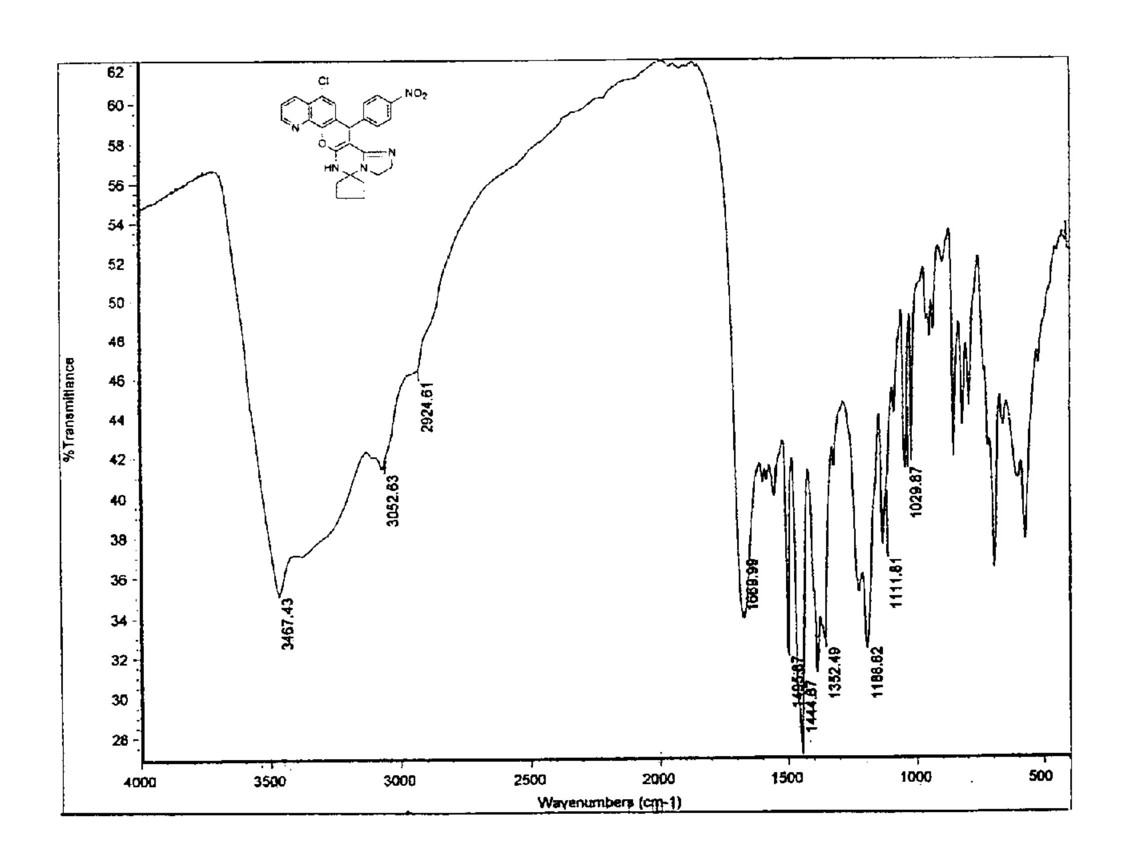


Fig.(59): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclopentane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(231$_c$)**.

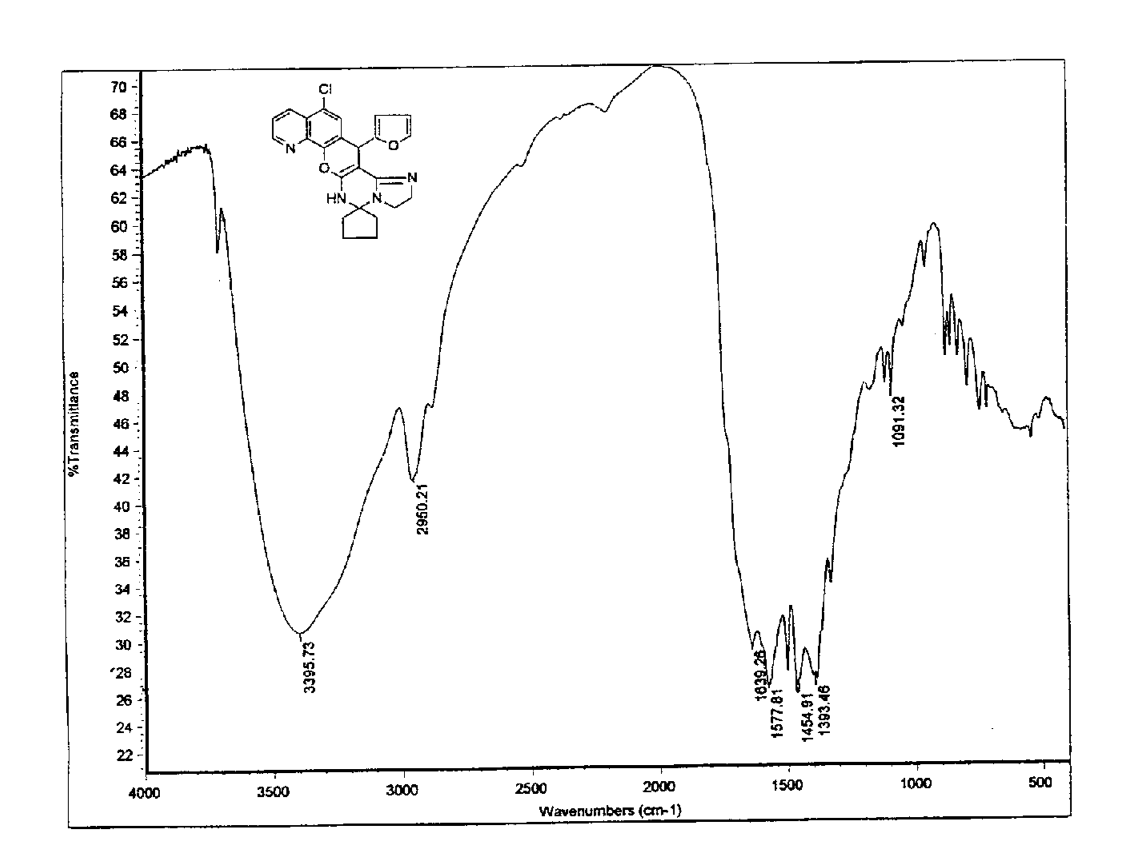


Fig.(60): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-spiro-(1'- cyclopentane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(231$_d$)**.

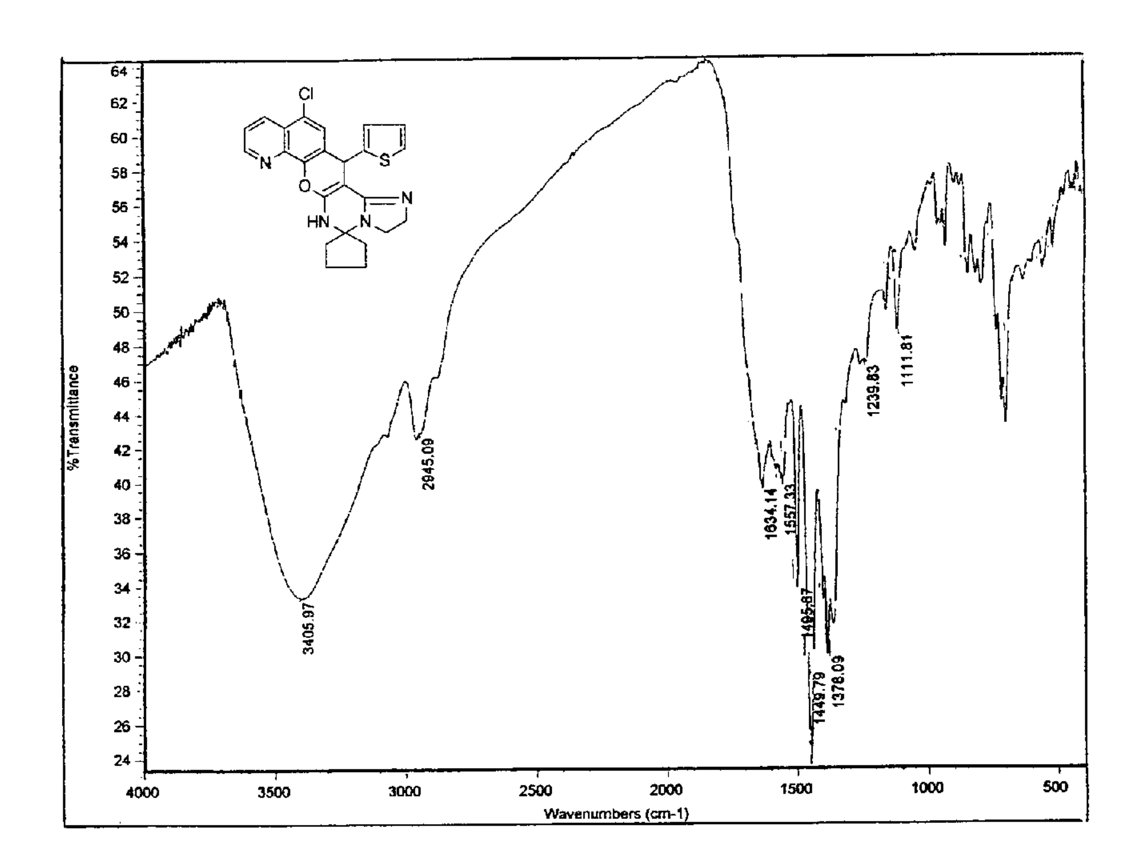


Fig.(61): 12-Chloro-14-thienyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclopentane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(231_e)**.

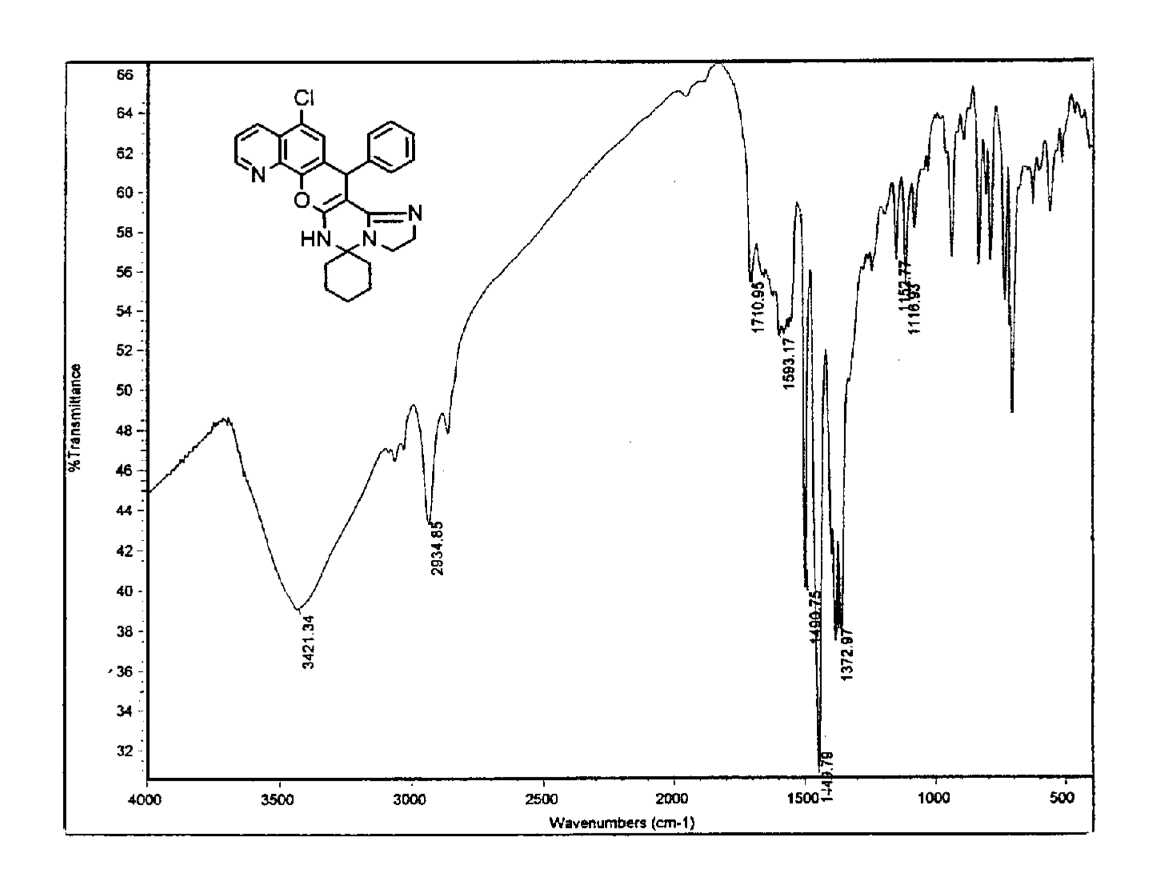


Fig.(62): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**232_a**).

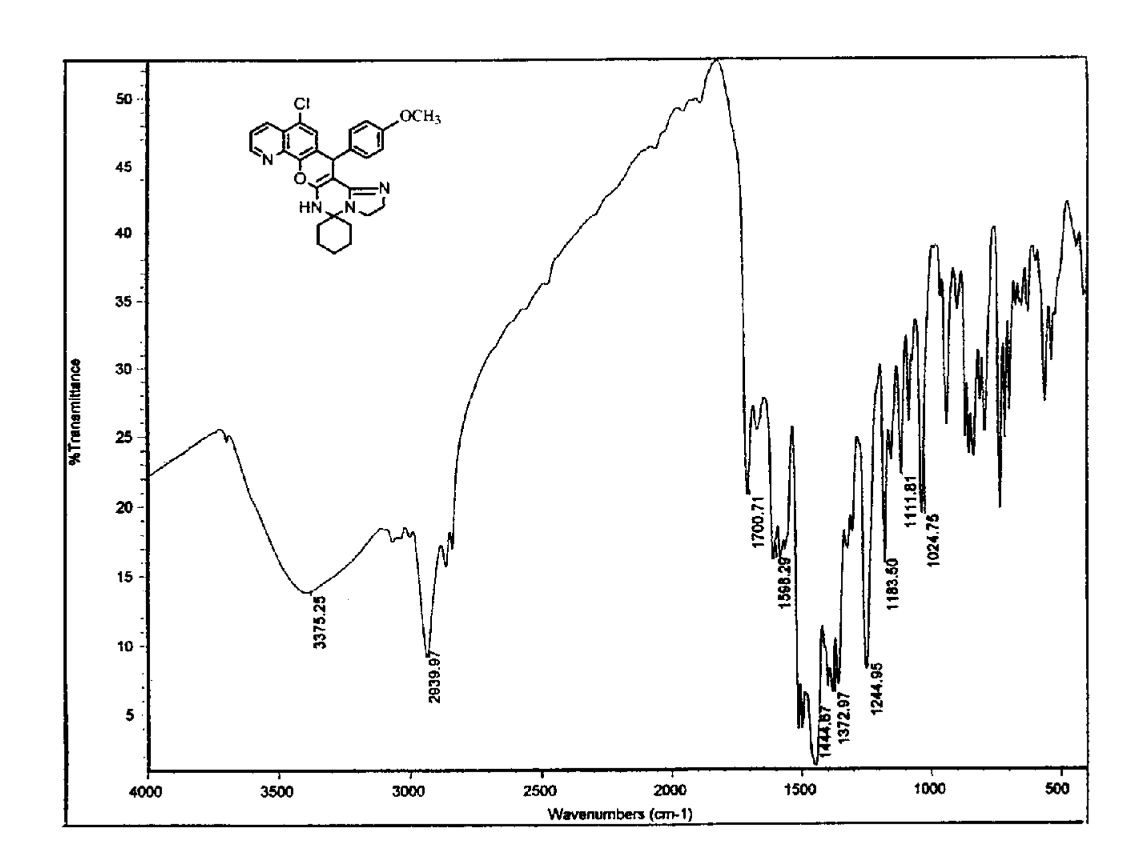


Fig.(63): 12-Chloro-14-(4-methoxy)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclohexane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(232$_b$)**.

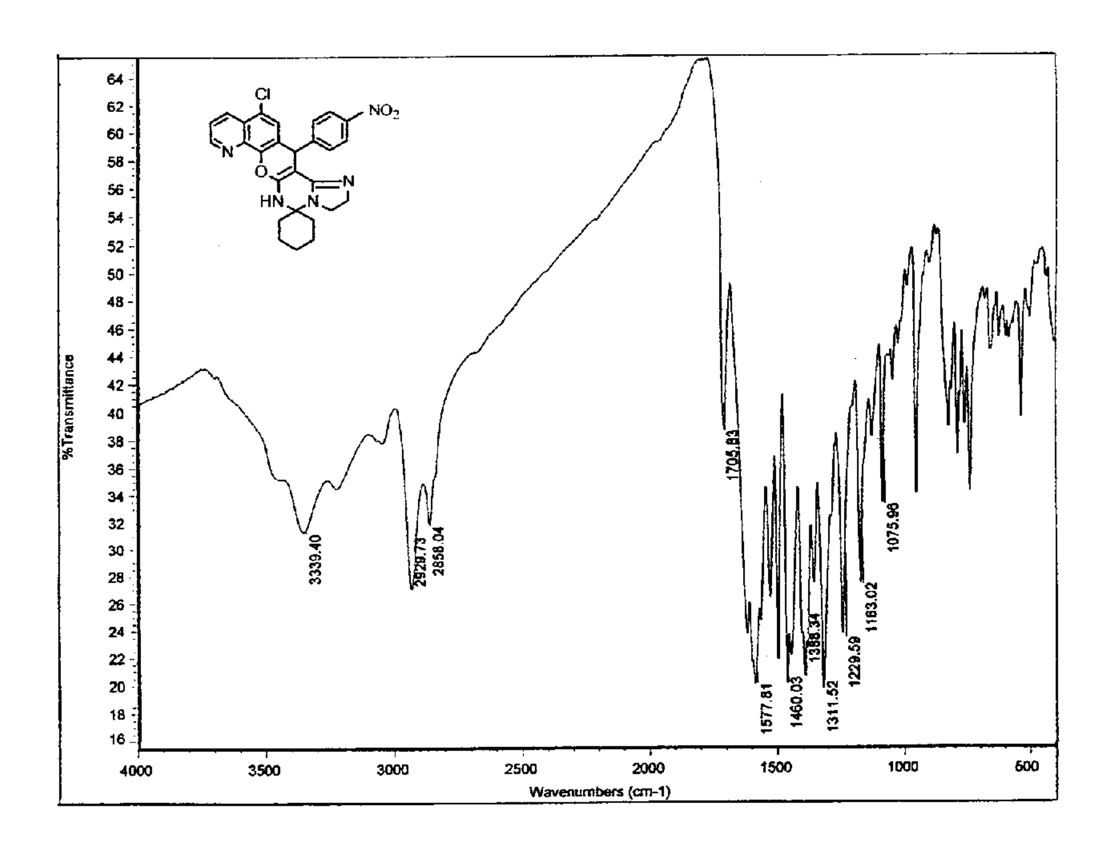


Fig.(64): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-spiro-(1'-cyclohexane)imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(232_c)**.

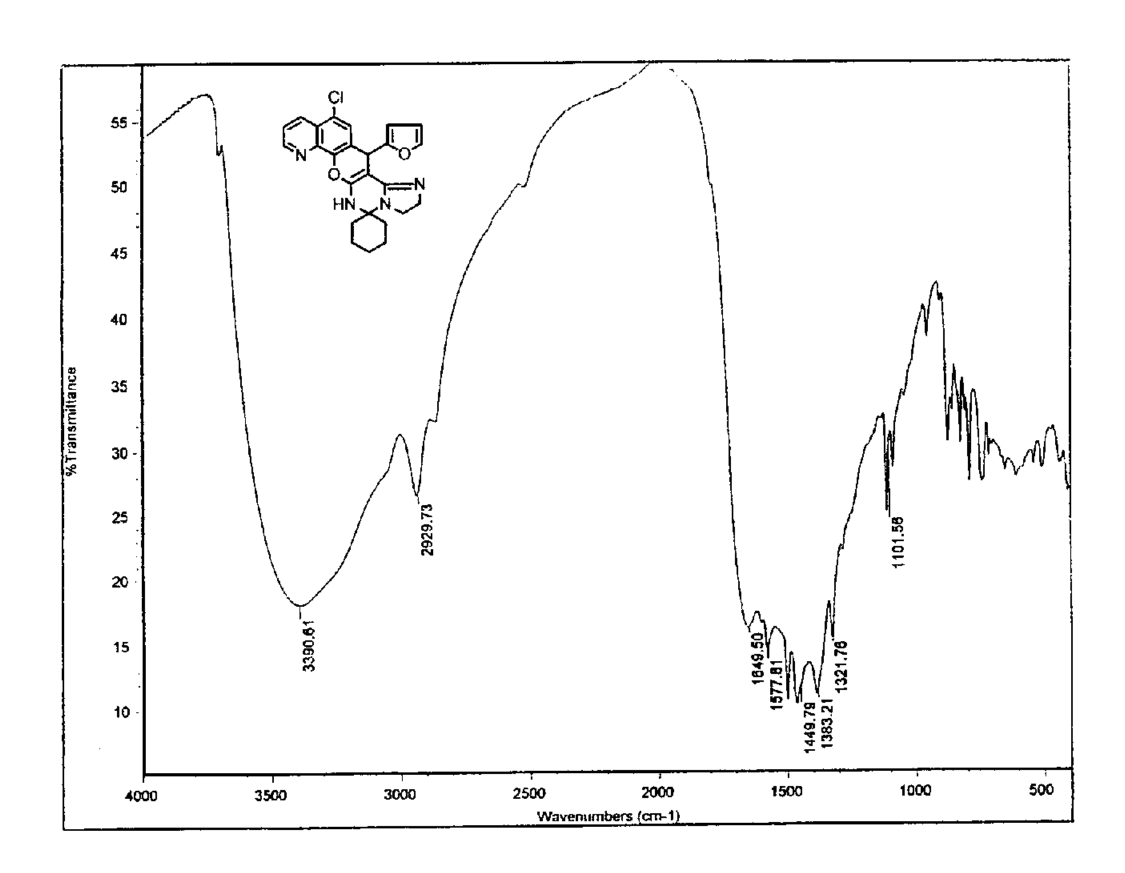


Fig.(65): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(232_d)**.

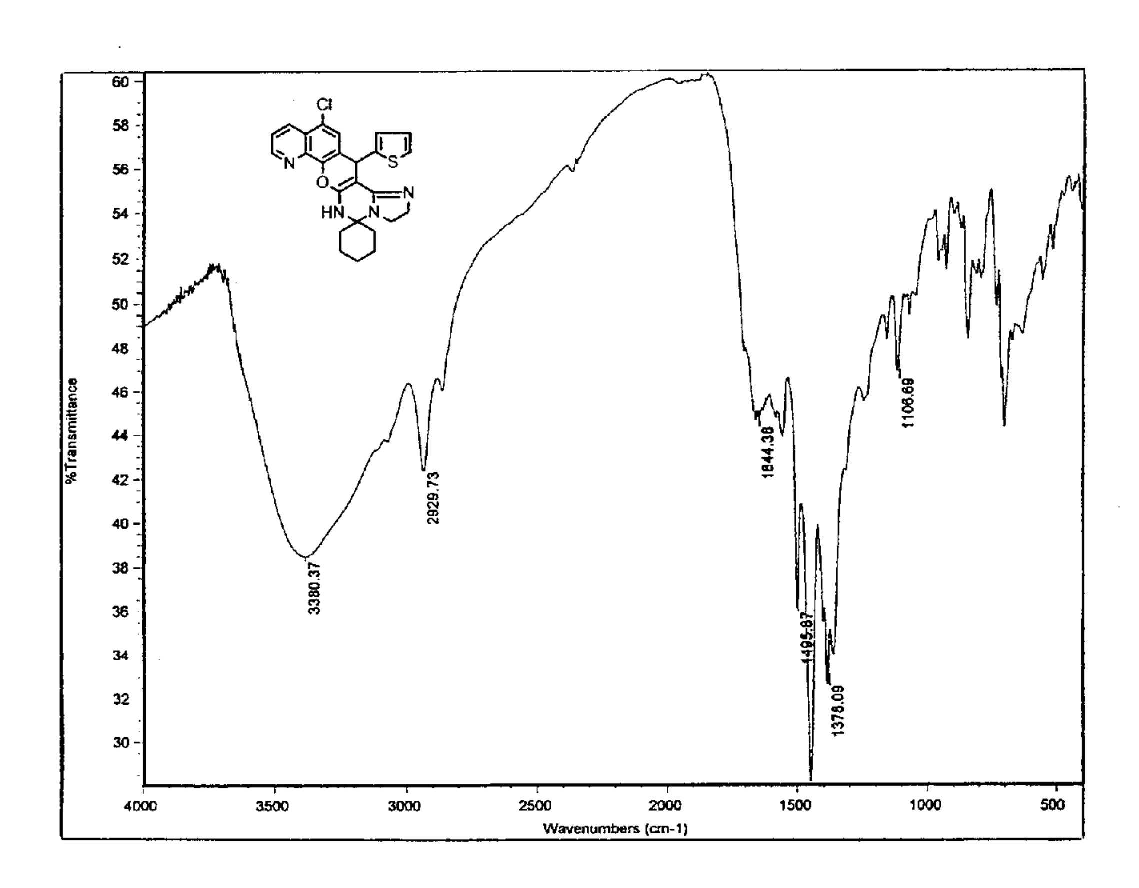
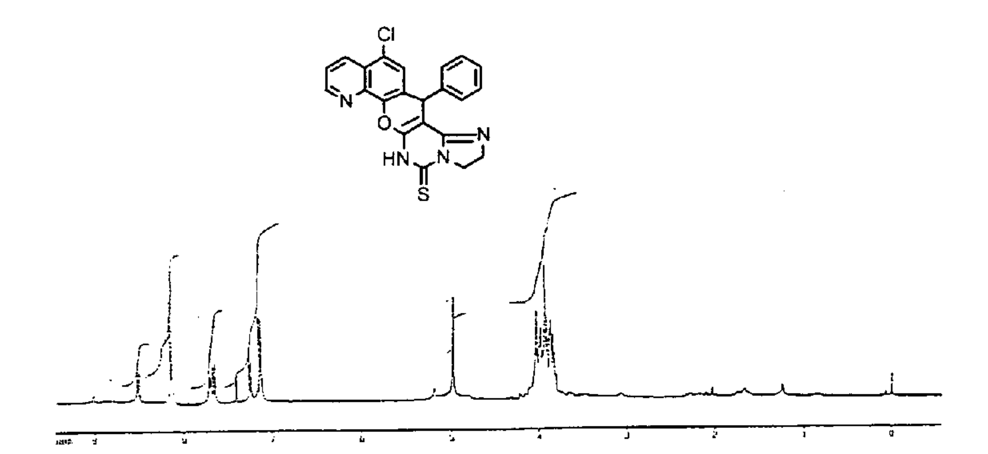


Fig.(66): 12-Chloro-14-thieyl-2,3,6,14-tetrahydro-5-spiro(1'-cyclohexane)-imidazo[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(232$_e$)**.



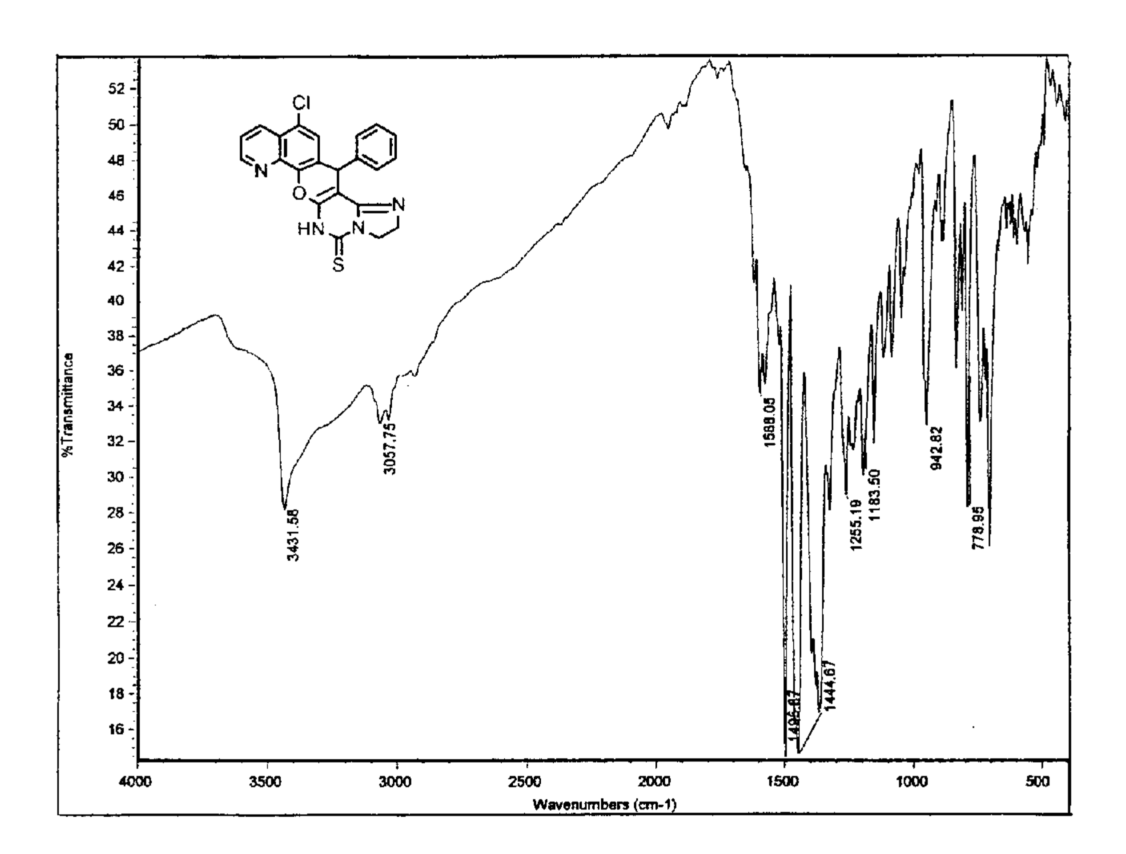


Fig.(67): 12-Chloro-14-phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(233$_a$)**.

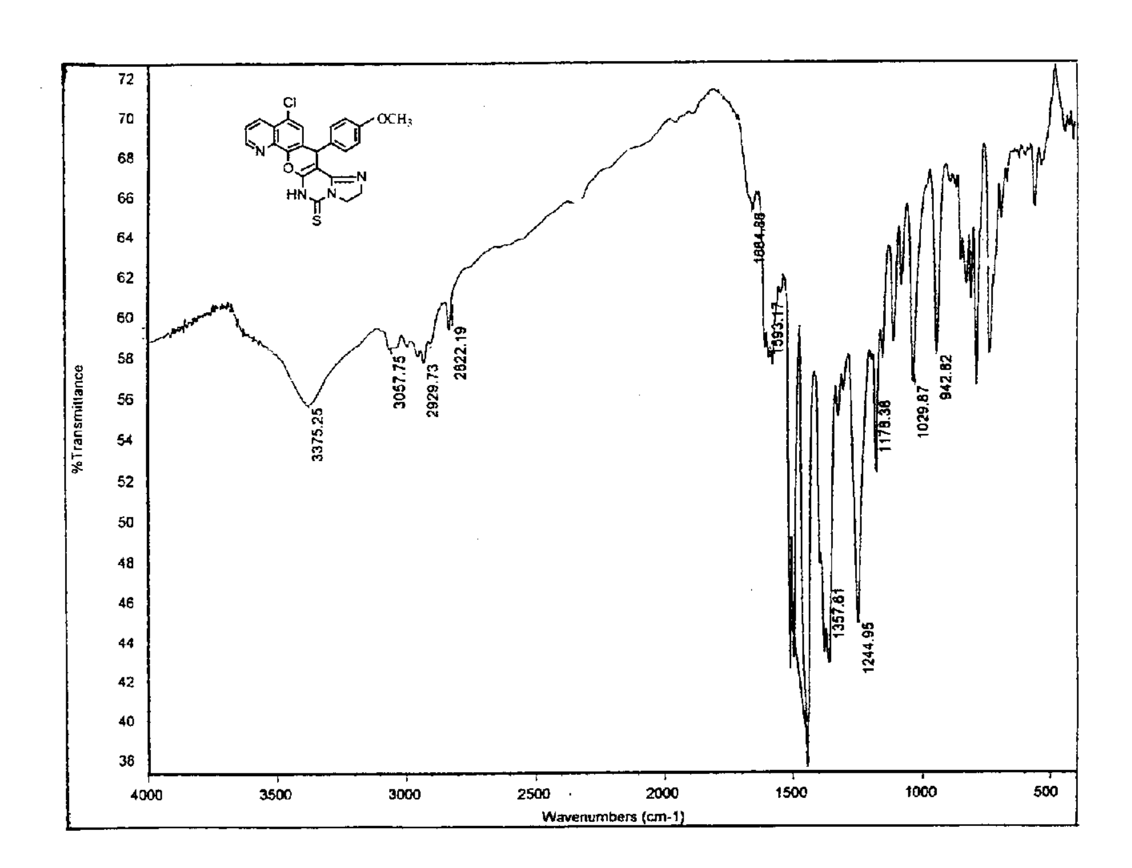


Fig.(68): 12-Chloro-14-(4-methoxy)phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline (**233$_b$**).

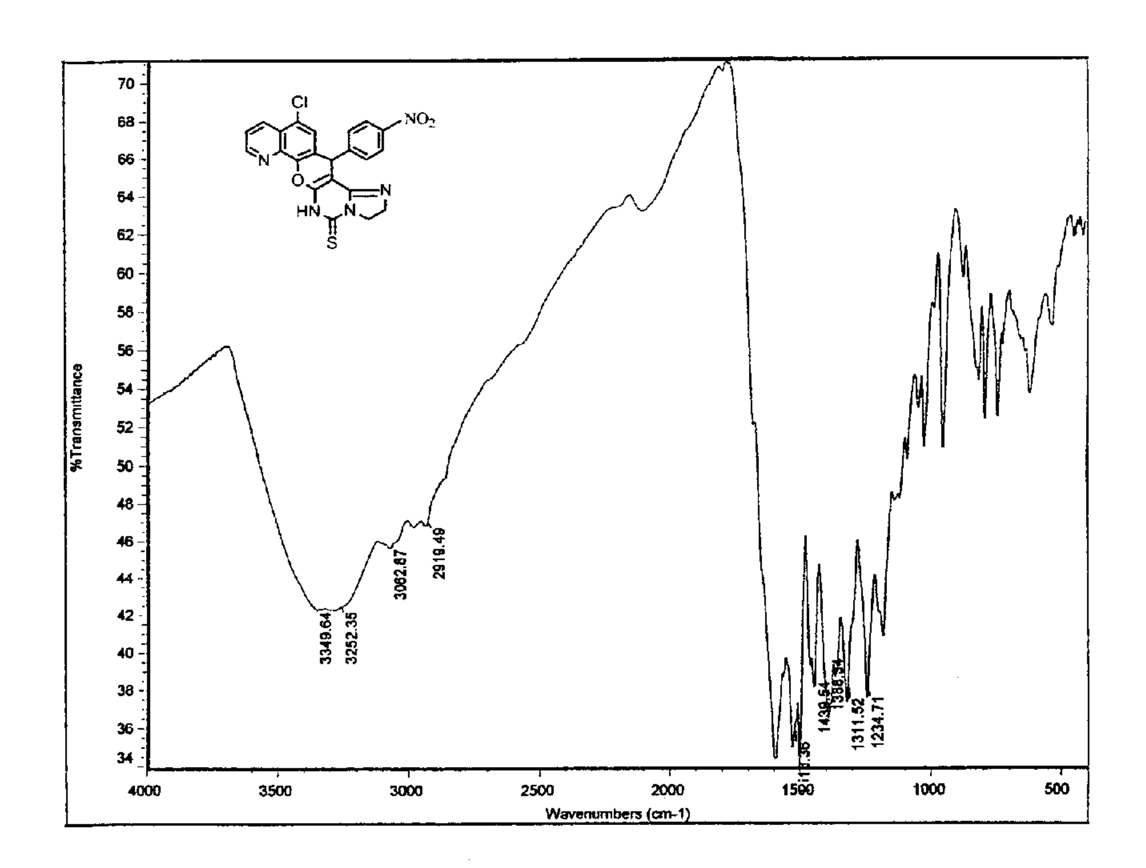


Fig.(69): 12-Chloro-14-(4-nitro)phenyl-2,3,6,14-tetrahydro-5-thioxoimidazo-[1,2-c]pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(233$_c$)**.

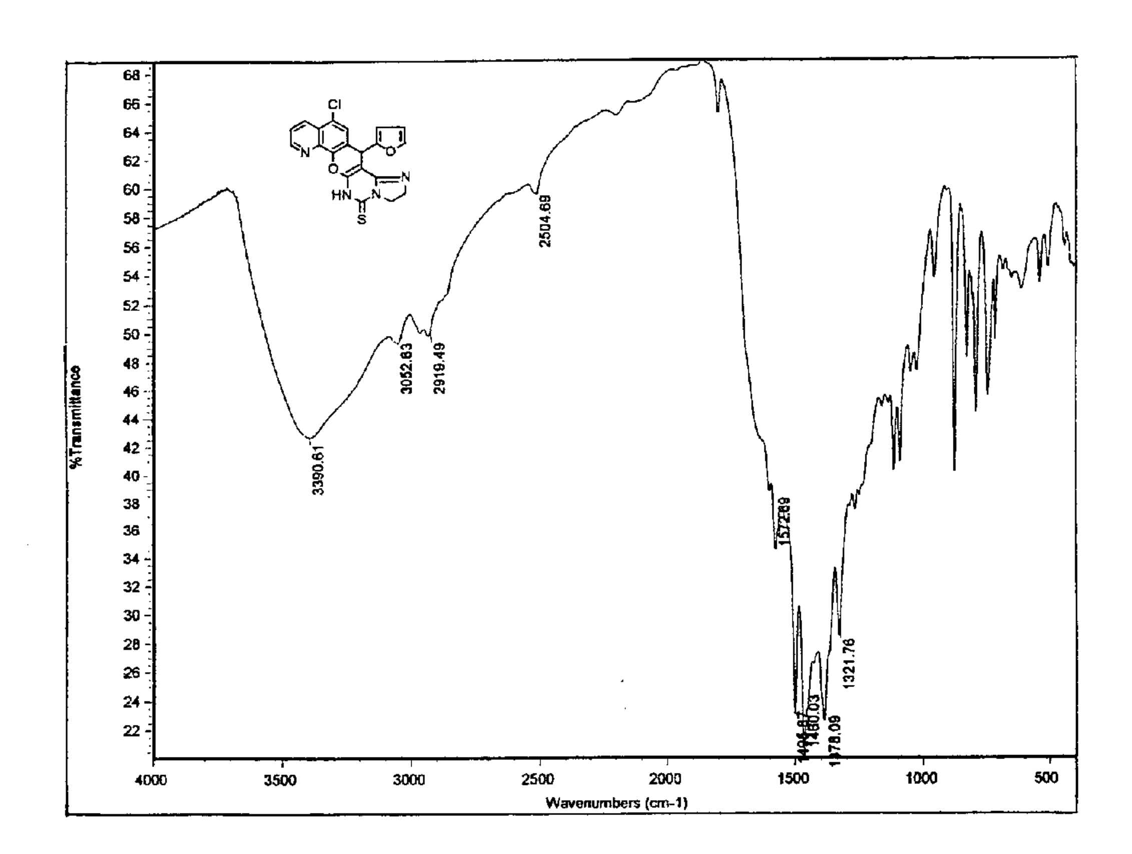


Fig.(70): 12-Chloro-14-furyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(233_d)**.

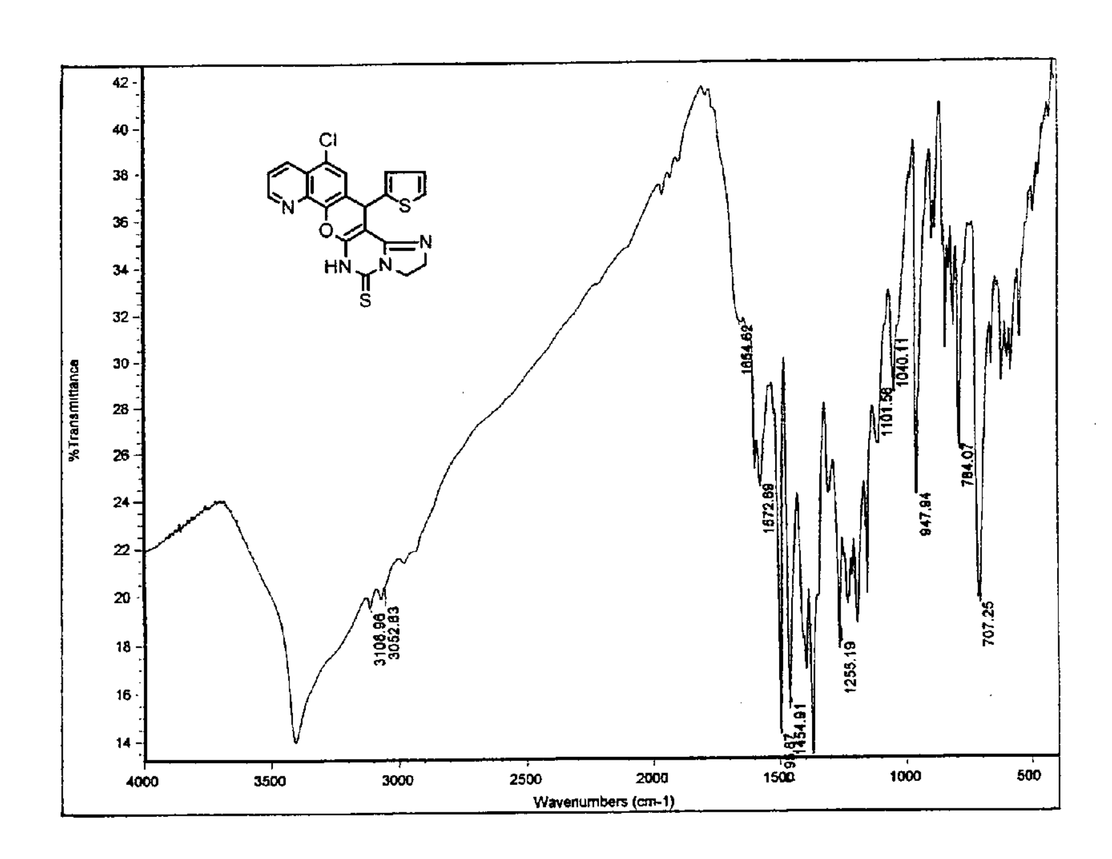
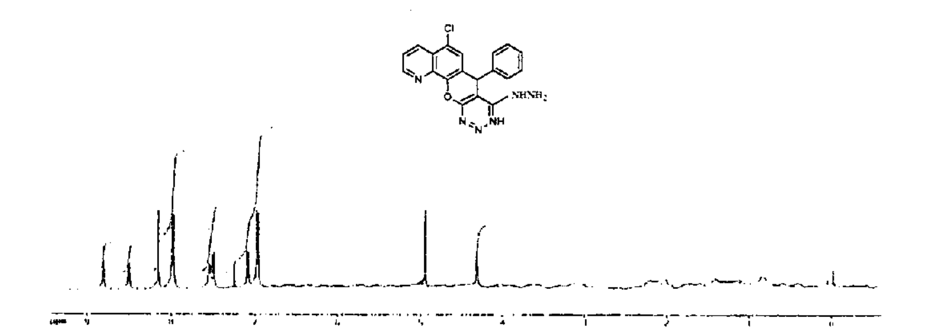


Fig.(71): 12-Chloro-14-thienyl-2,3,6,14-tetrahydro-5-thioxoimidazo[1,2-c]-pyrimido[4',5':6,5]pyrano[3,2-h]quinoline **(233$_e$)**.



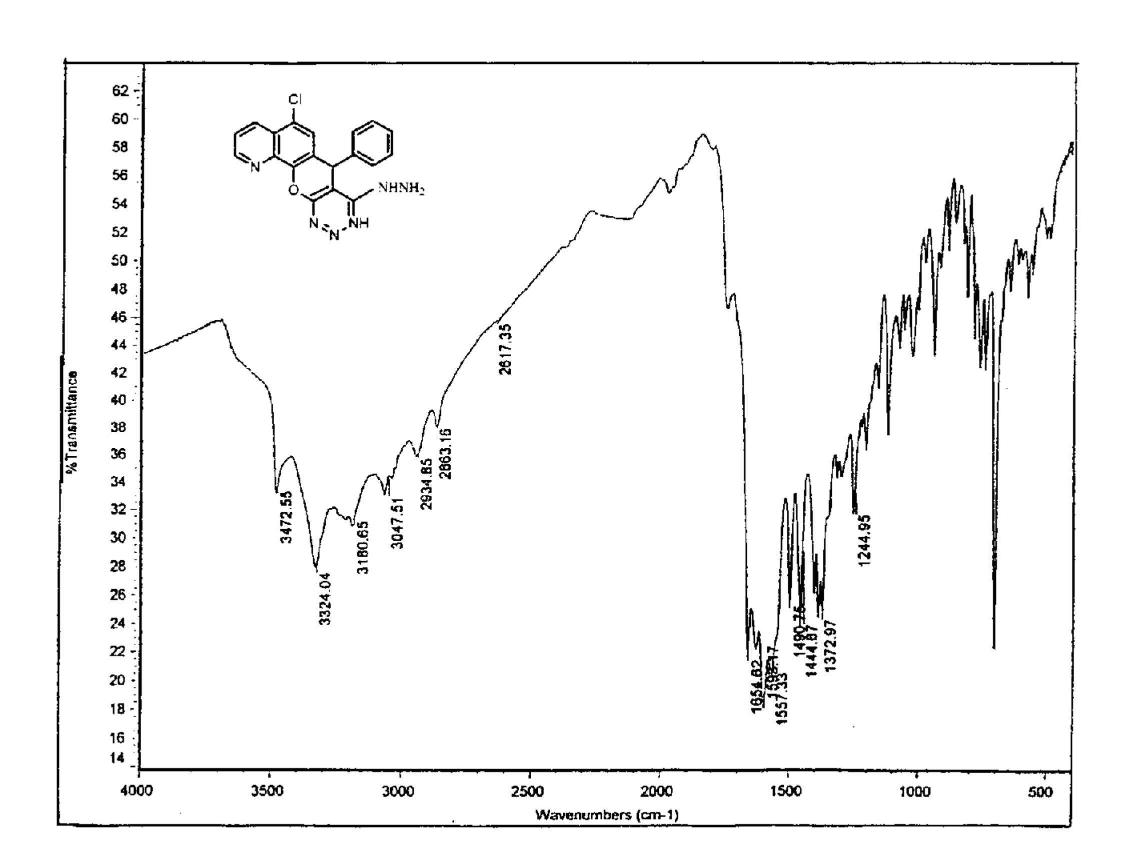


Fig.(72): 7-Chloro-5-phenyl-5H-4-hydrazino-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline **(234$_a$)**.

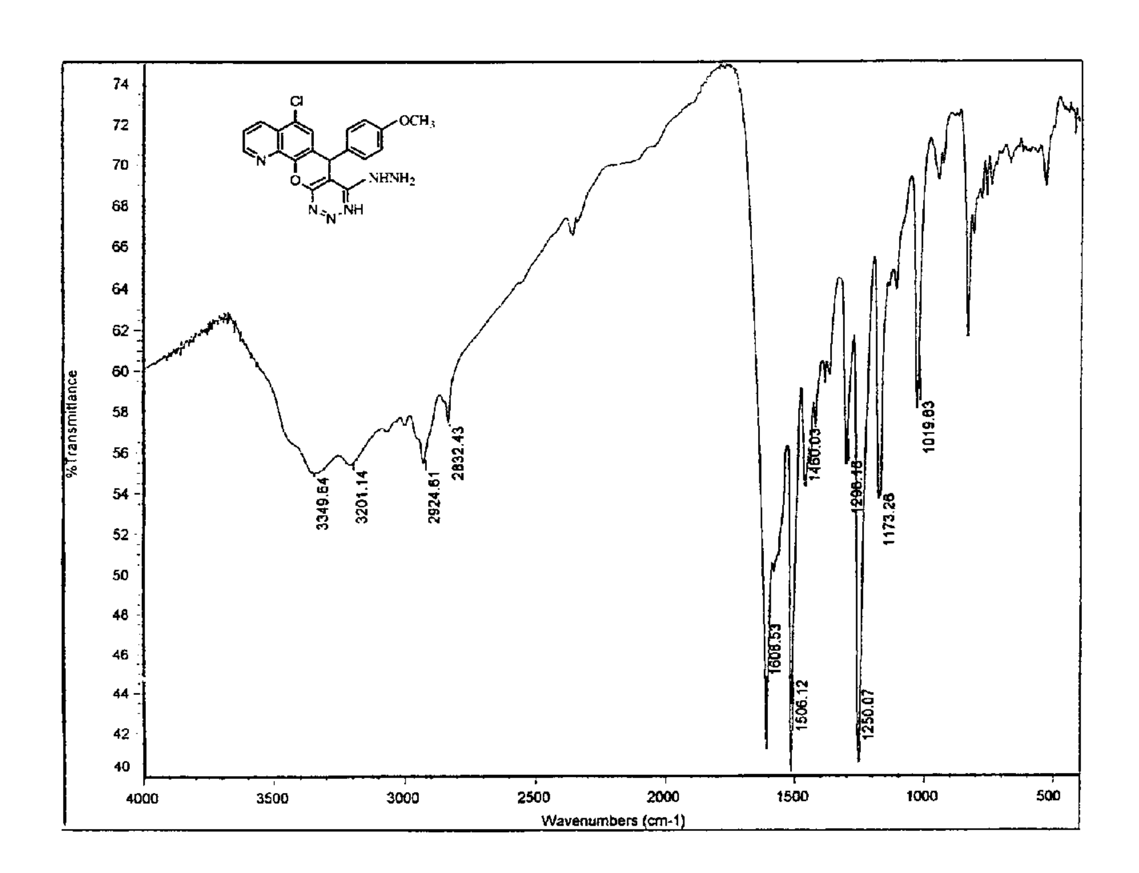


Fig.(73): 7-Chloro-5-(4-methoxy)phenyl-5H-4-hydrazino-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline **(234_b)**.

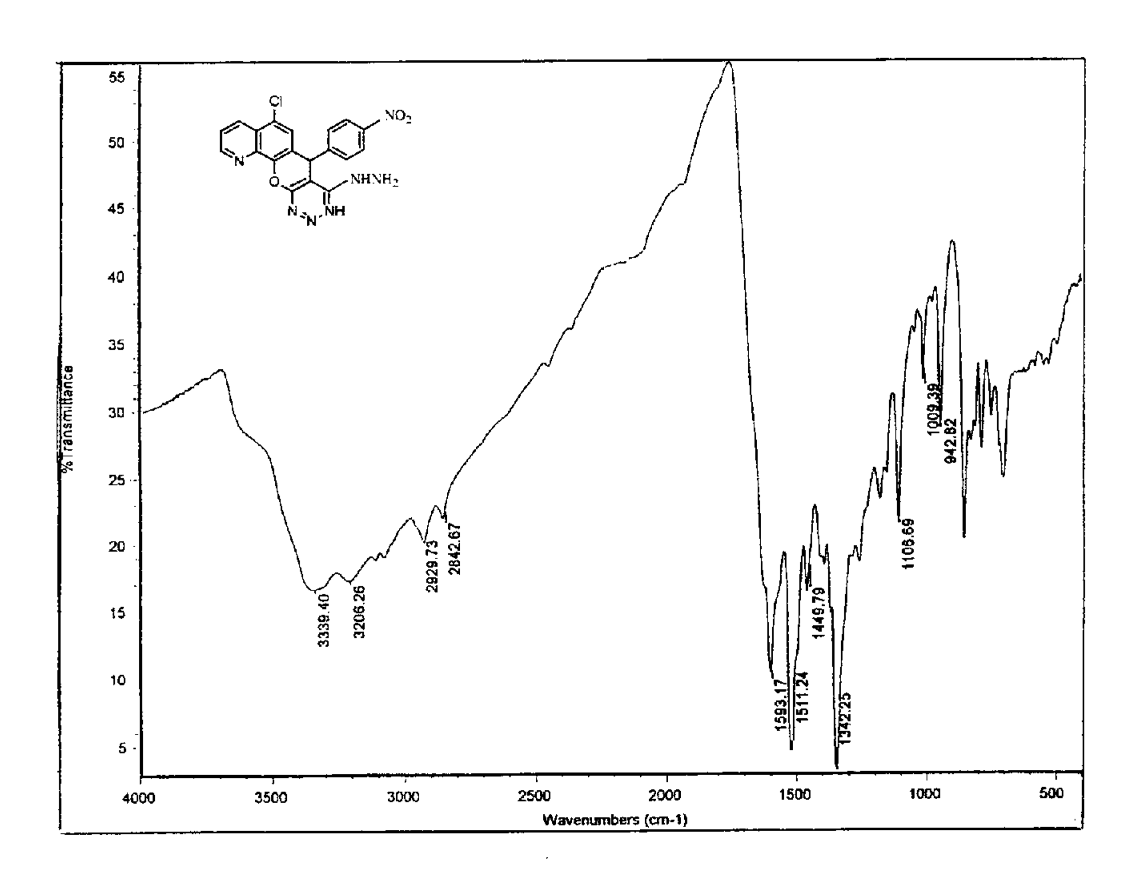


Fig.(74): 7-Chloro-5-(4-nitro)phenyl-5H-4-hydrazino-1,2,3-triazino-[4',5':6,5]pyrano[3.2-h]quinoline **(234$_c$)**.

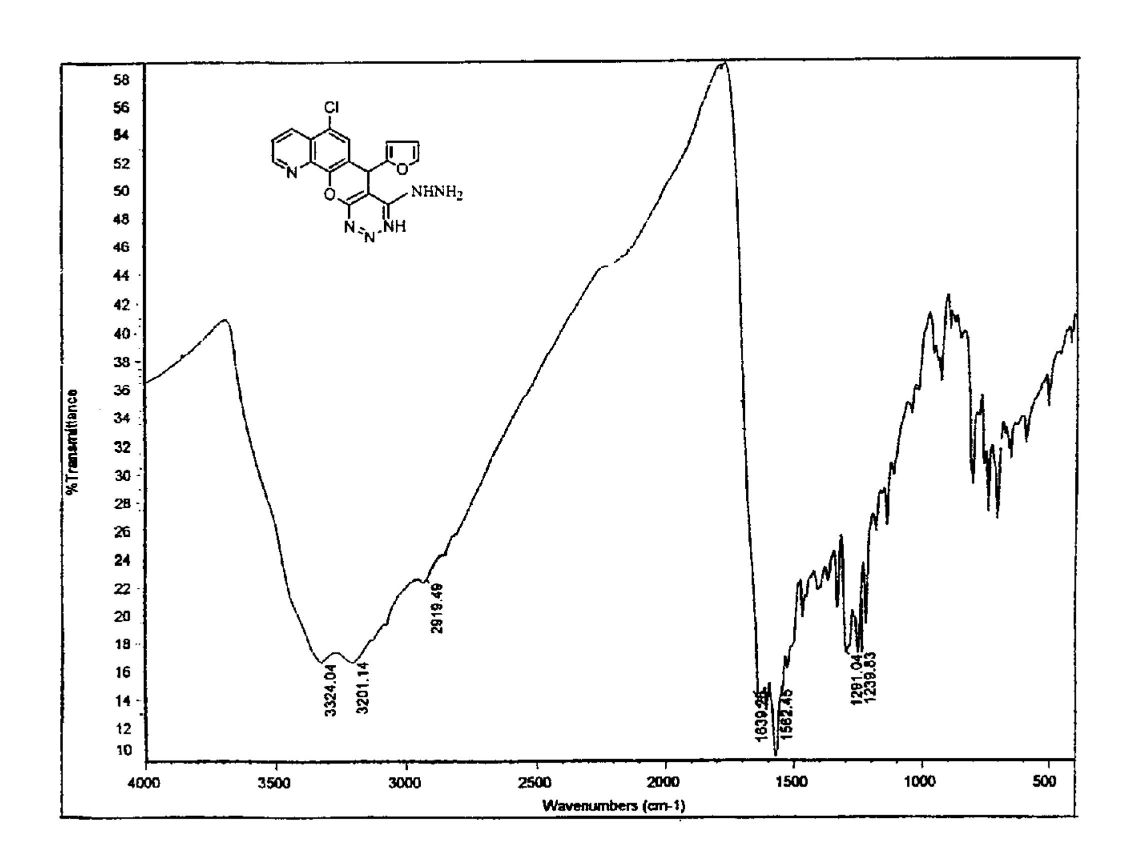
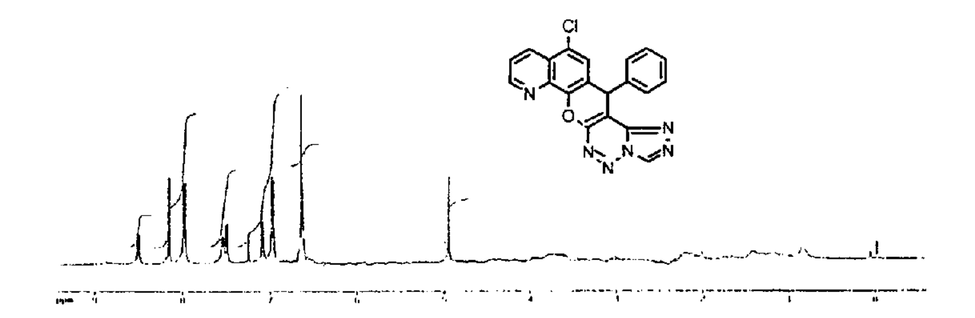


Fig.(75): 7-Chloro-5-furyl-5H-4-hydrazino-1,2,3-triazino[4',5':6,5]pyrano - [3,2-h]quinoline **(234$_d$)**.



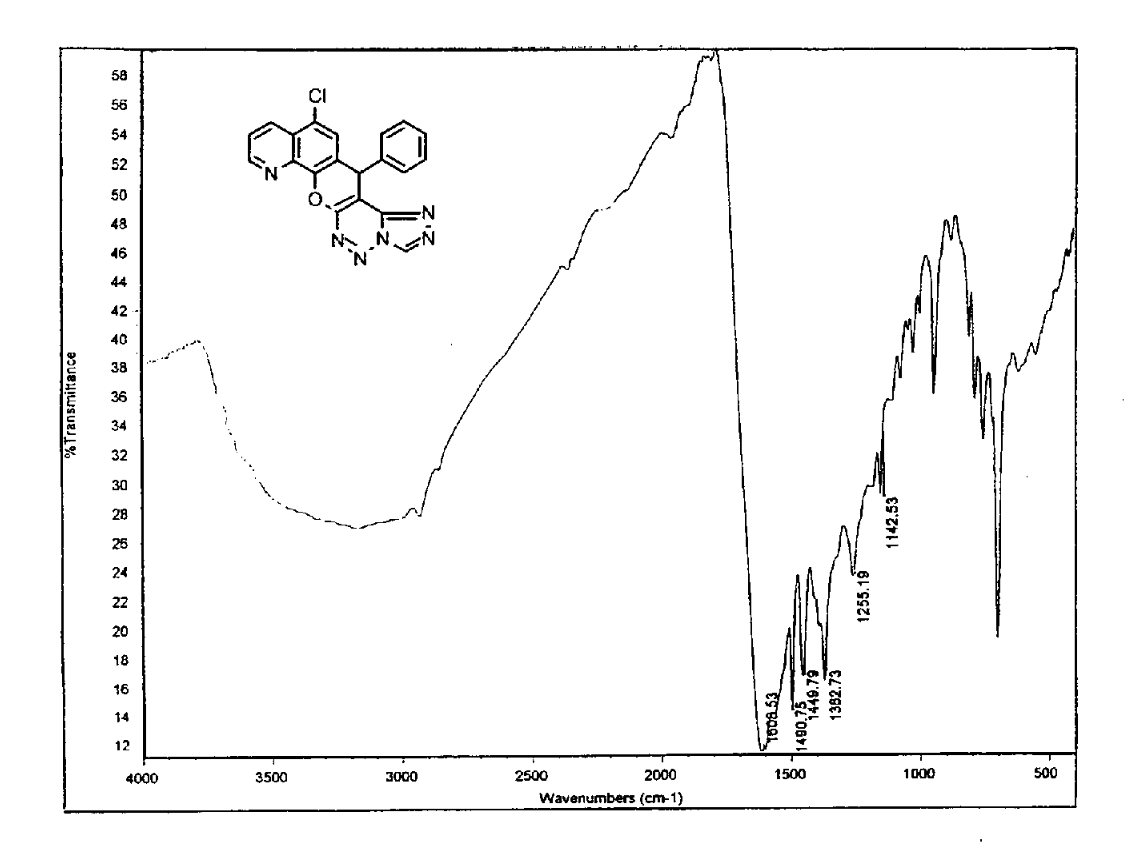


Fig.(76): 12-Chloro-14-phenyl-14H-1,2,4-triazolo[3",4"-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline **(235_a)**.

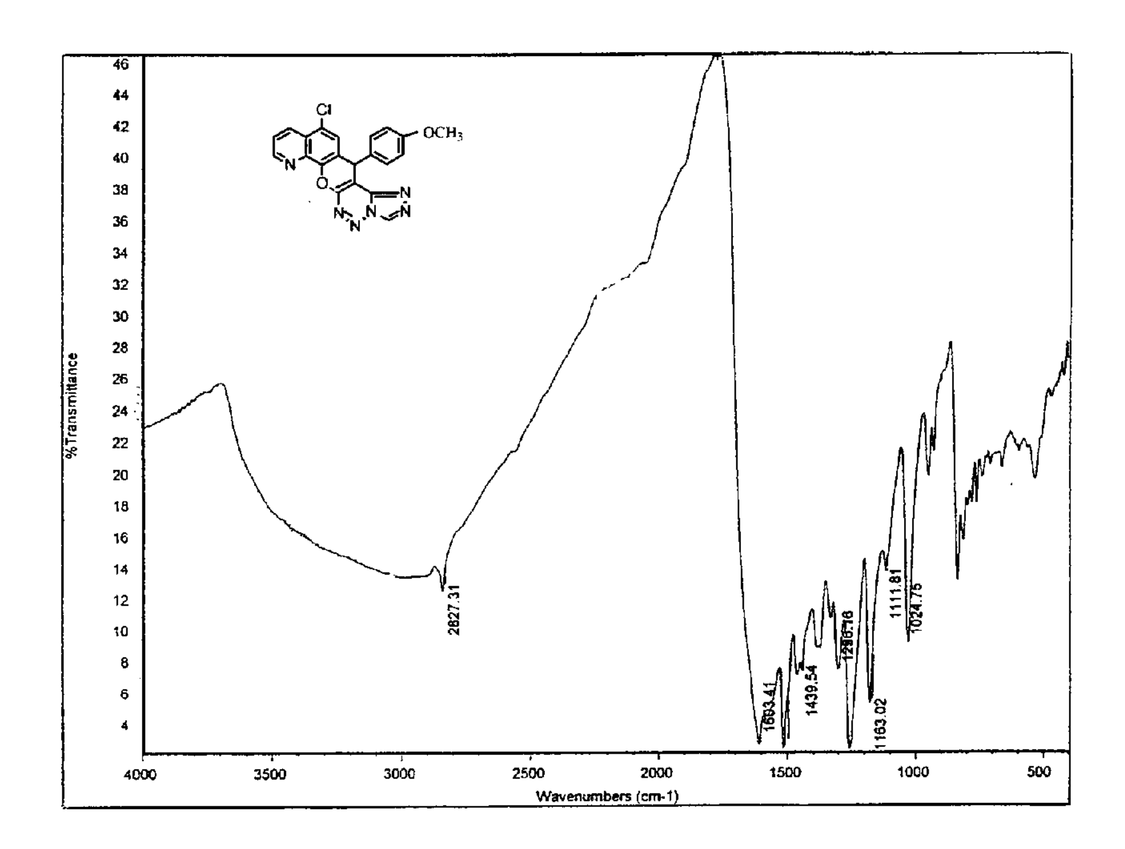


Fig.(77): 12-Chloro-14-(4-methoxy)phenyl-14H-1,2,4-triazolo[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(235_b)**.

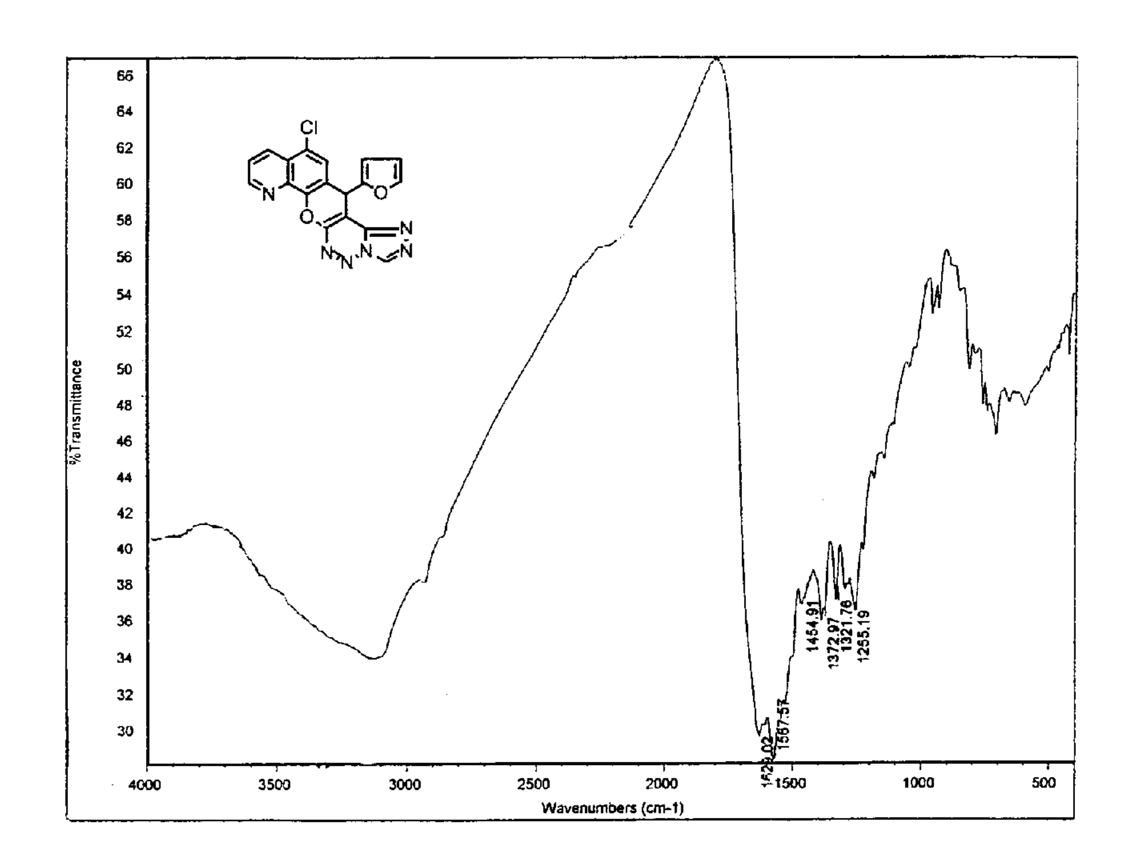


Fig.(78): 12-Chloro-14-furyl-14H-1,2,4-triazolo[3",4"-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline (**235_d**).

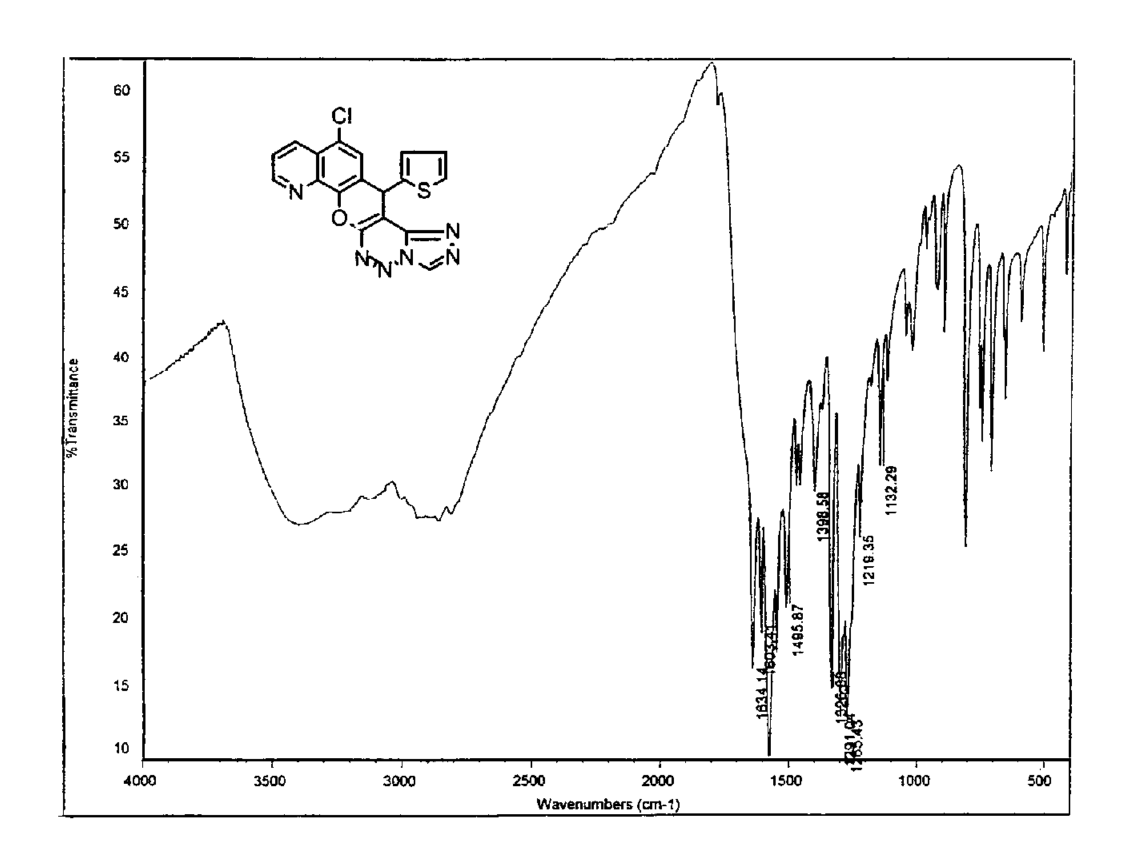
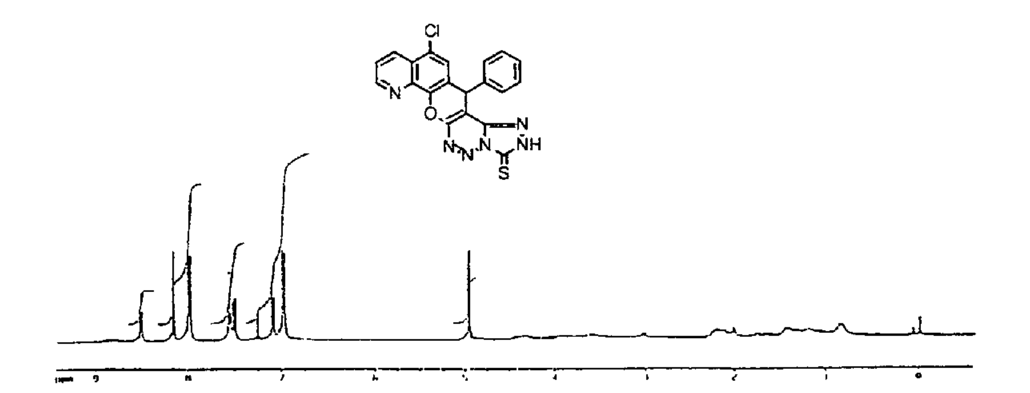


Fig.(79): 12-Chloro-14-thienyl-14H-1,2,4-triazolo[3",4"-f]-1,2,3-triazino-[4',5':6,5]pyrano[3,2-h]quinoline **(235$_e$)**.



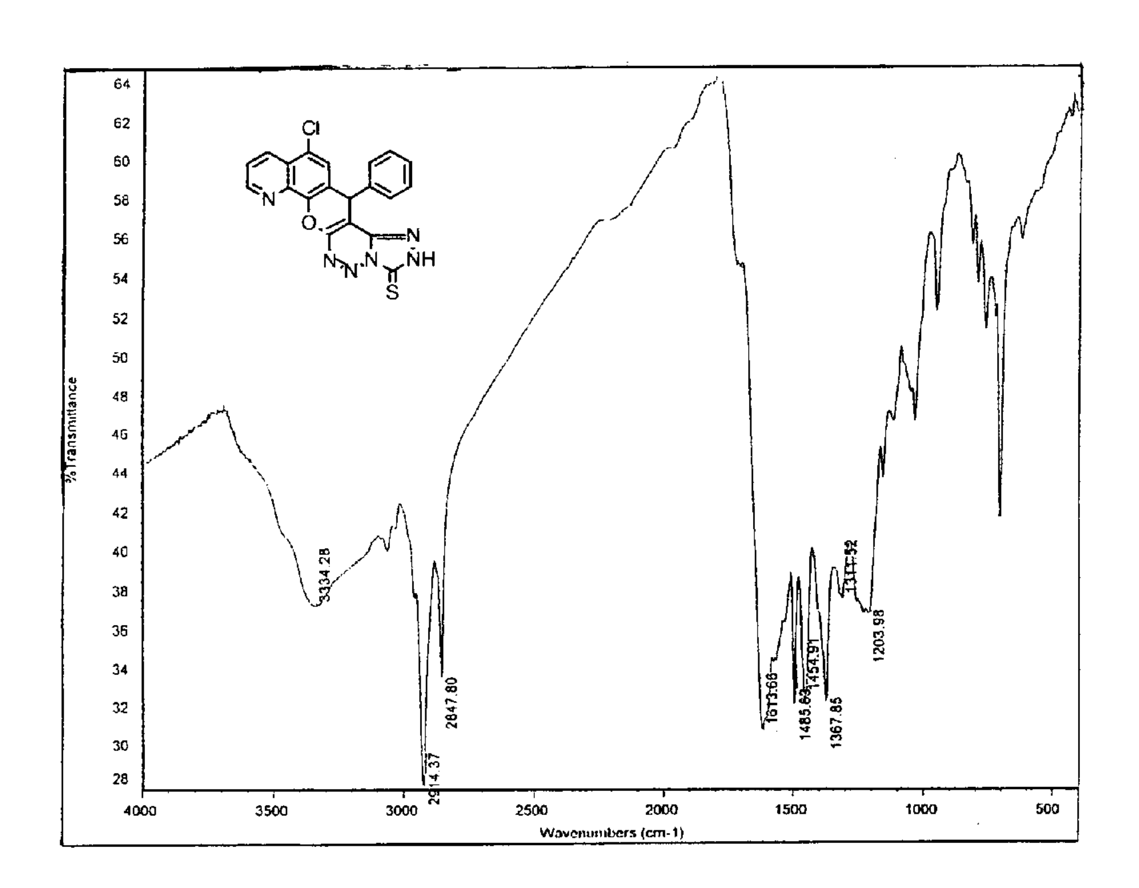


Fig.(80): 12-Chloro-14-phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(236_a)**.

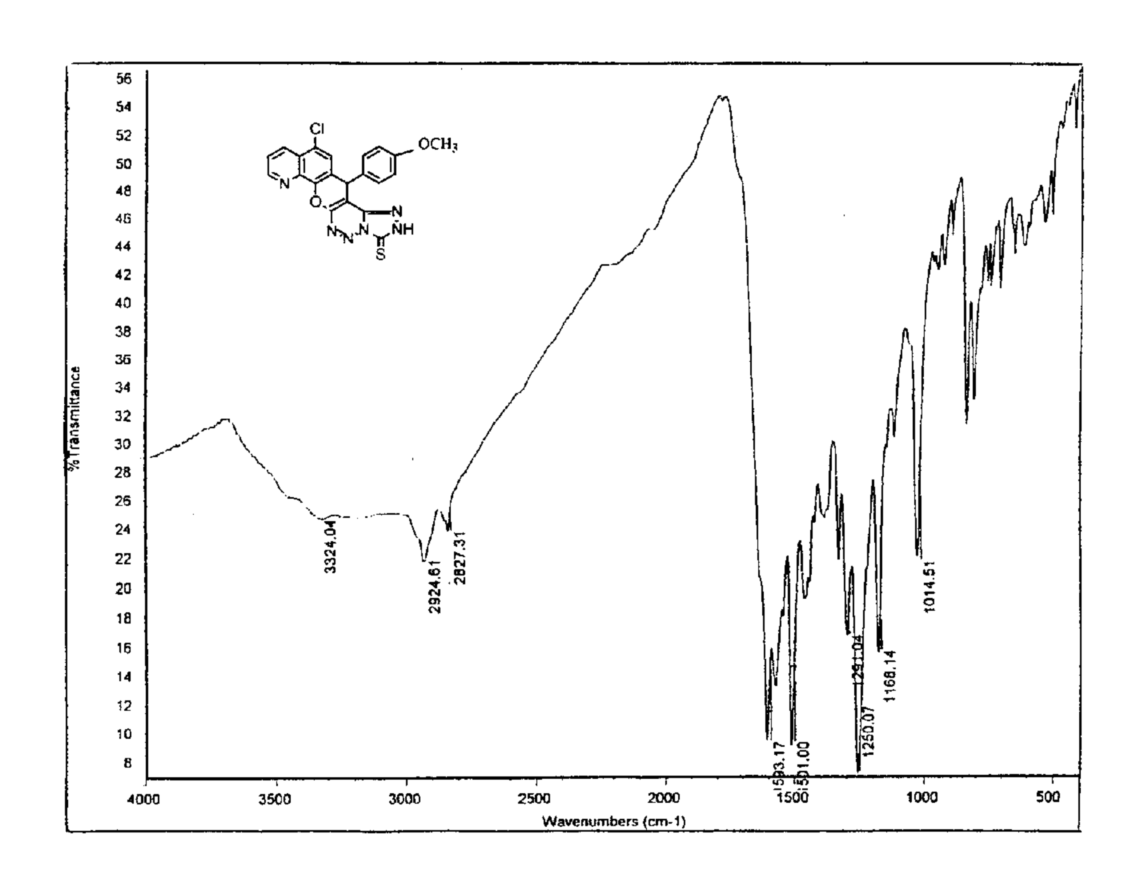


Fig.(81): 12-Chloro-14-(4-methoxy)phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo-[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(236_b)**.

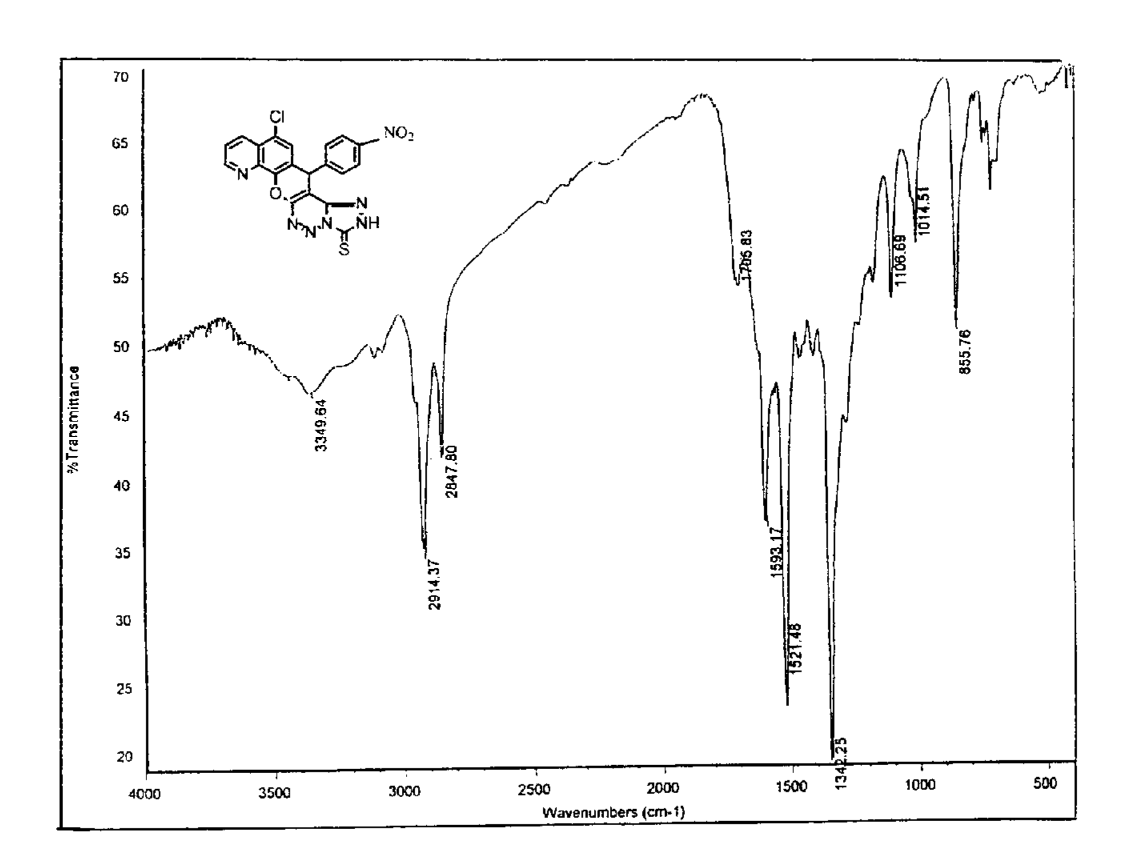


Fig.(82): 12-Chloro-14-(4-nitro)phenyl-2,14-dihydro-3-thioxo-1,2,4-triazolo-[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(236_c)**.

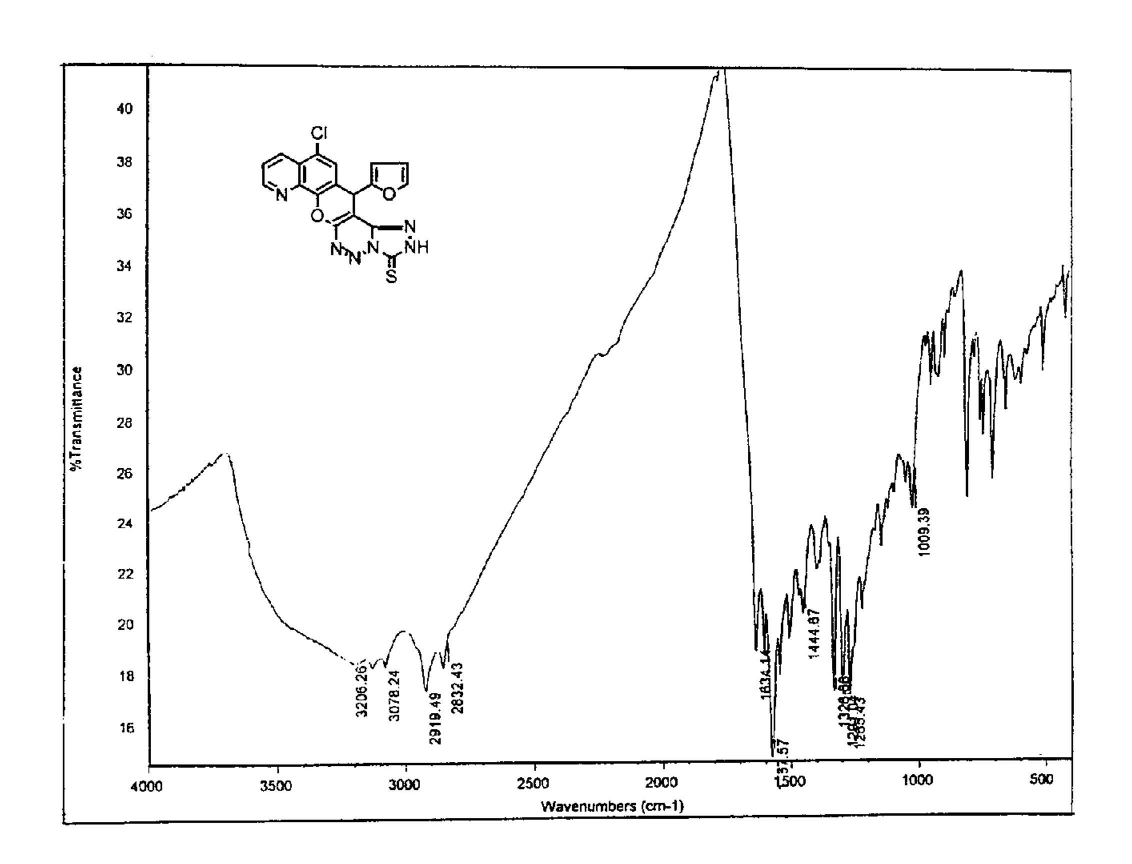


Fig.(83): 12-Chloro-14-furyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(236$_d$)**.

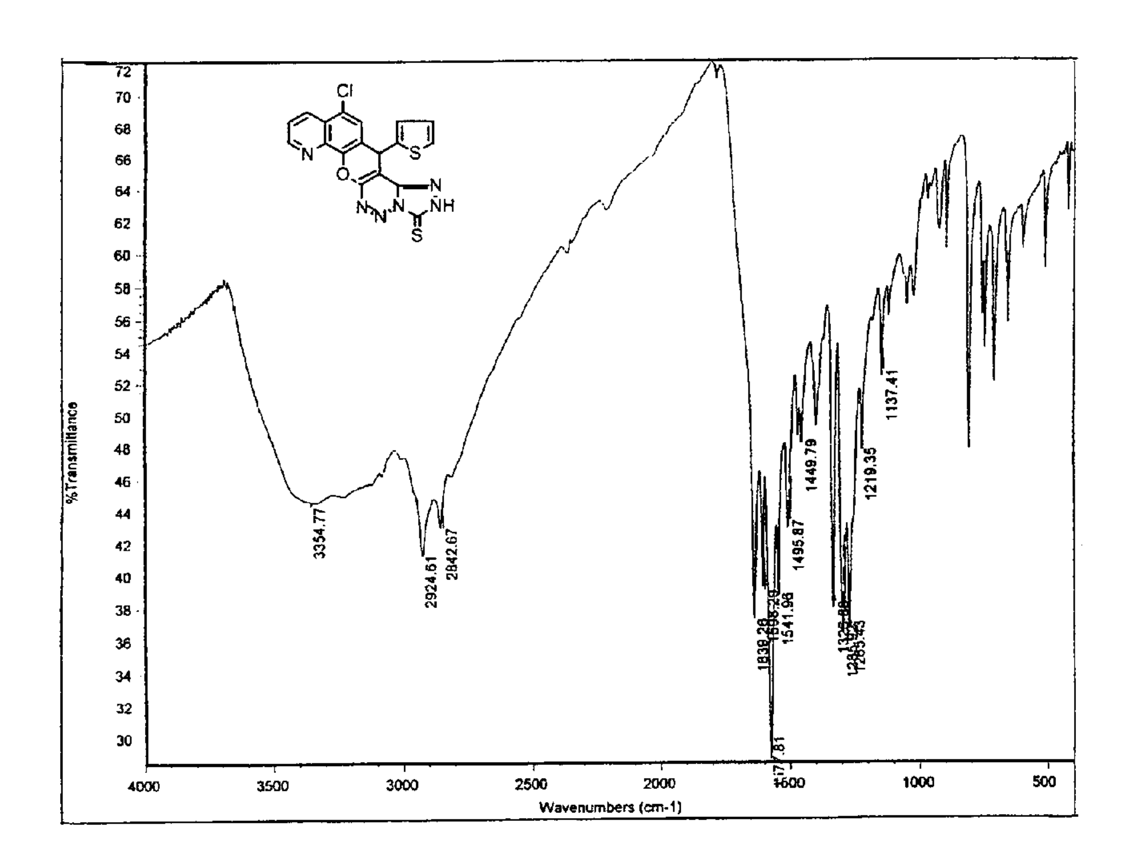


Fig.(84): 12-Chloro-14-thienyl-2,14-dihydro-3-thioxo-1,2,4-triazolo[3",4"-f]-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]quinoline **(236$_e$)**.

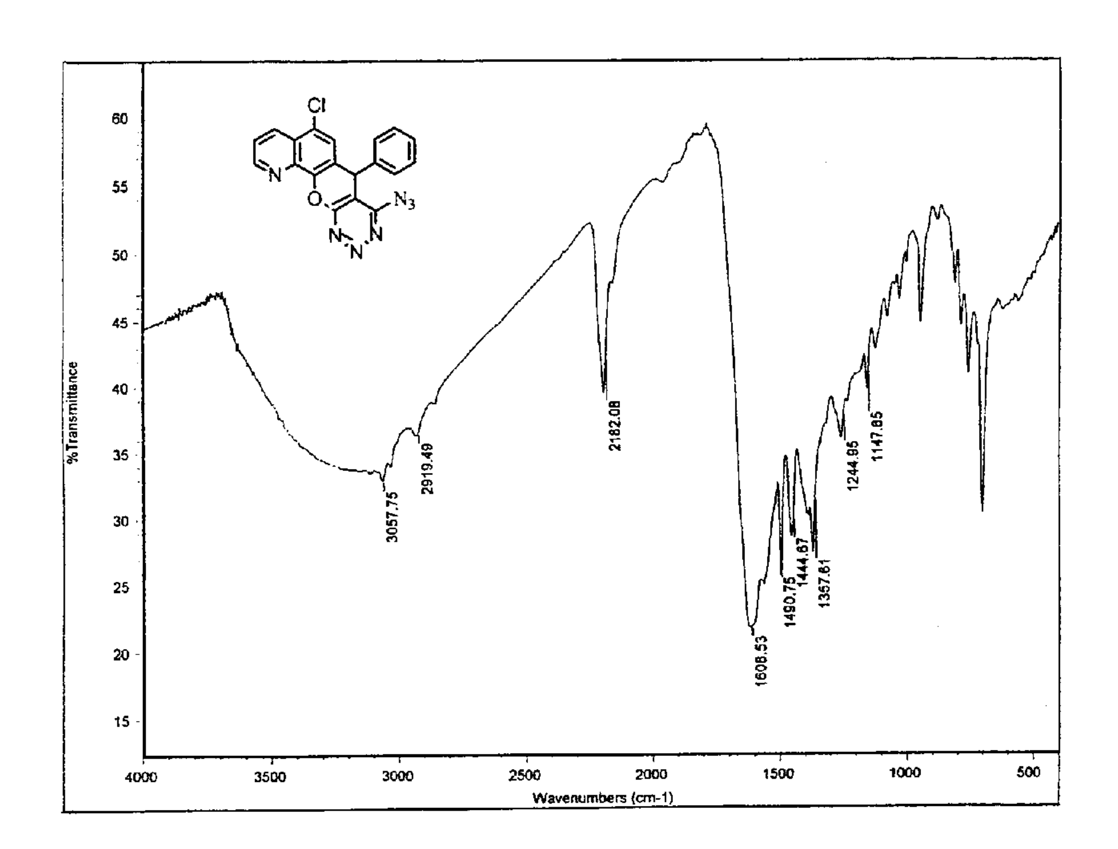


Fig.(85): 4-Azido-7-chloro-5-phenyl-5H-1,2,3-triazino[4',5':6,5]pyrano[3,2-h]-quinoline **(237_a)**.

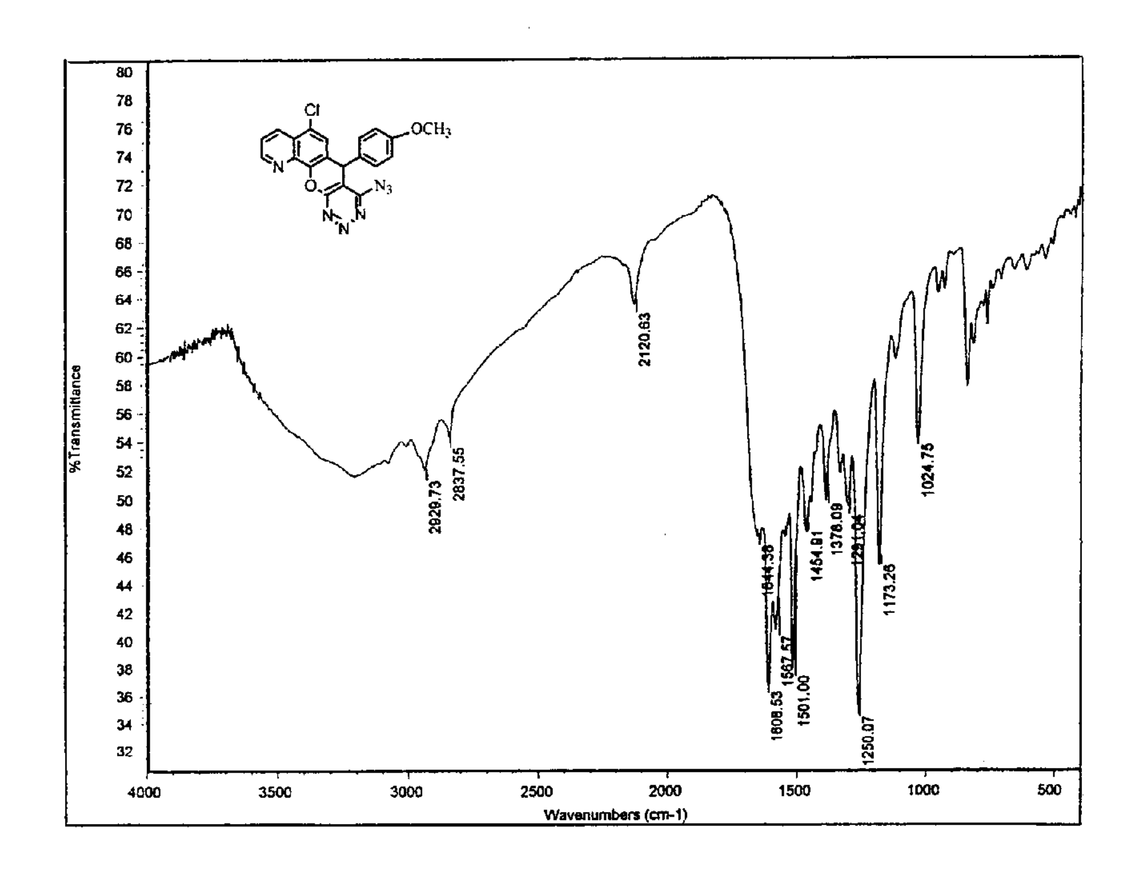


Fig.(86): 4-Azido-7-chloro-5-(4-methoxy)phenyl-5H-1,2,3-triazino[4',5':6,5]-pyrano[3,2-h]quinoline **(237_b)**.

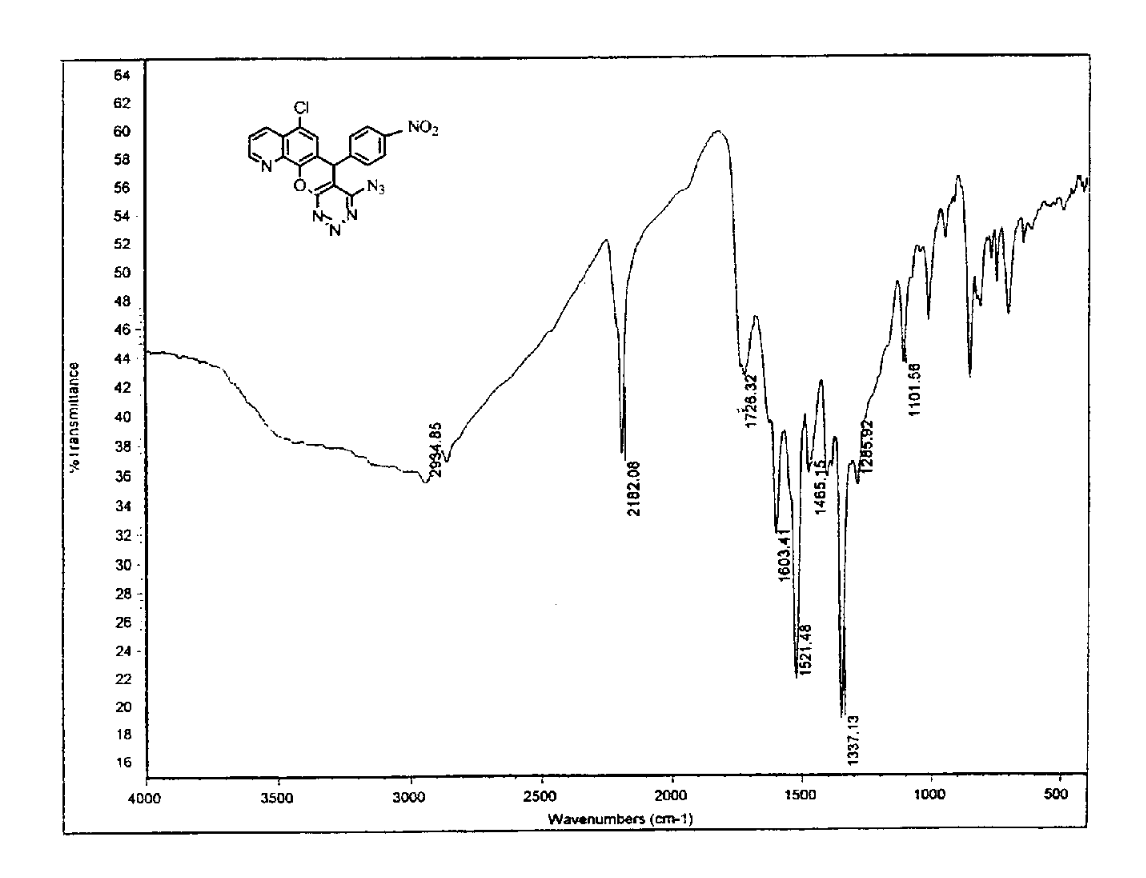


Fig.(87): 4-Azido-7-chloro-5-(4-nitro)phenyl-5H-1,2,3-triazino[4',5':6,5]-pyrano[3,2-h]quinoline **(237_c)**.

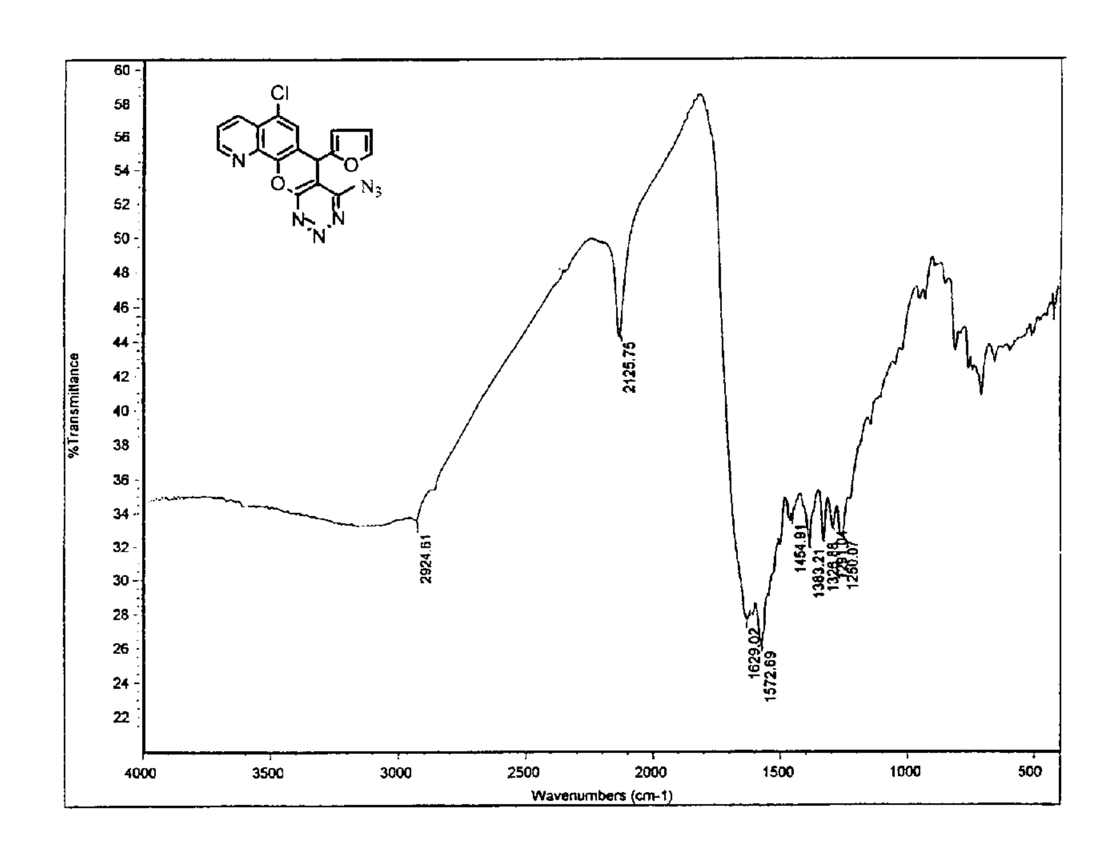


Fig.(88): 4-Azido-7-chloro-5-furyl-5H-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline (**237_d**).

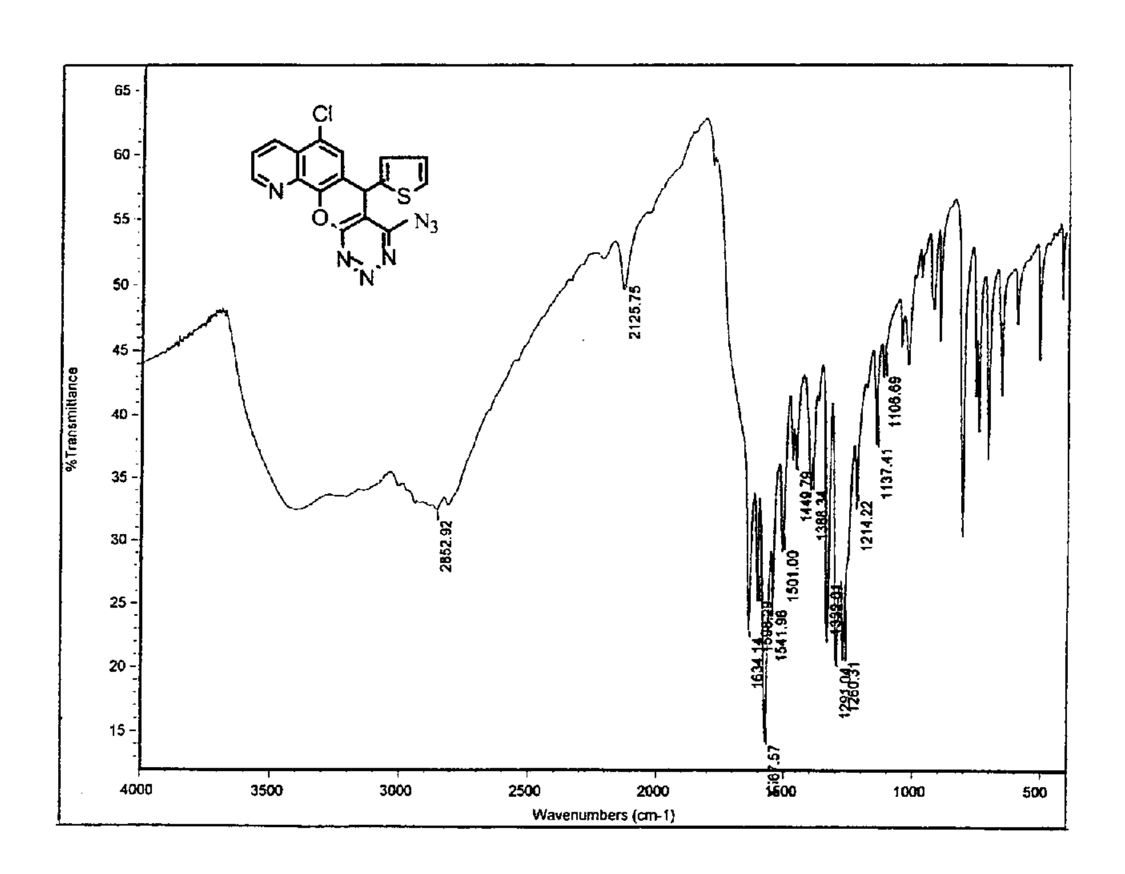


Fig.(89): 4-Azido-7-chloro-5-thienyl-5H-1,2,3-triazino[4',5':6,5]pyrano-[3,2-h]quinoline **(237$_e$)**.

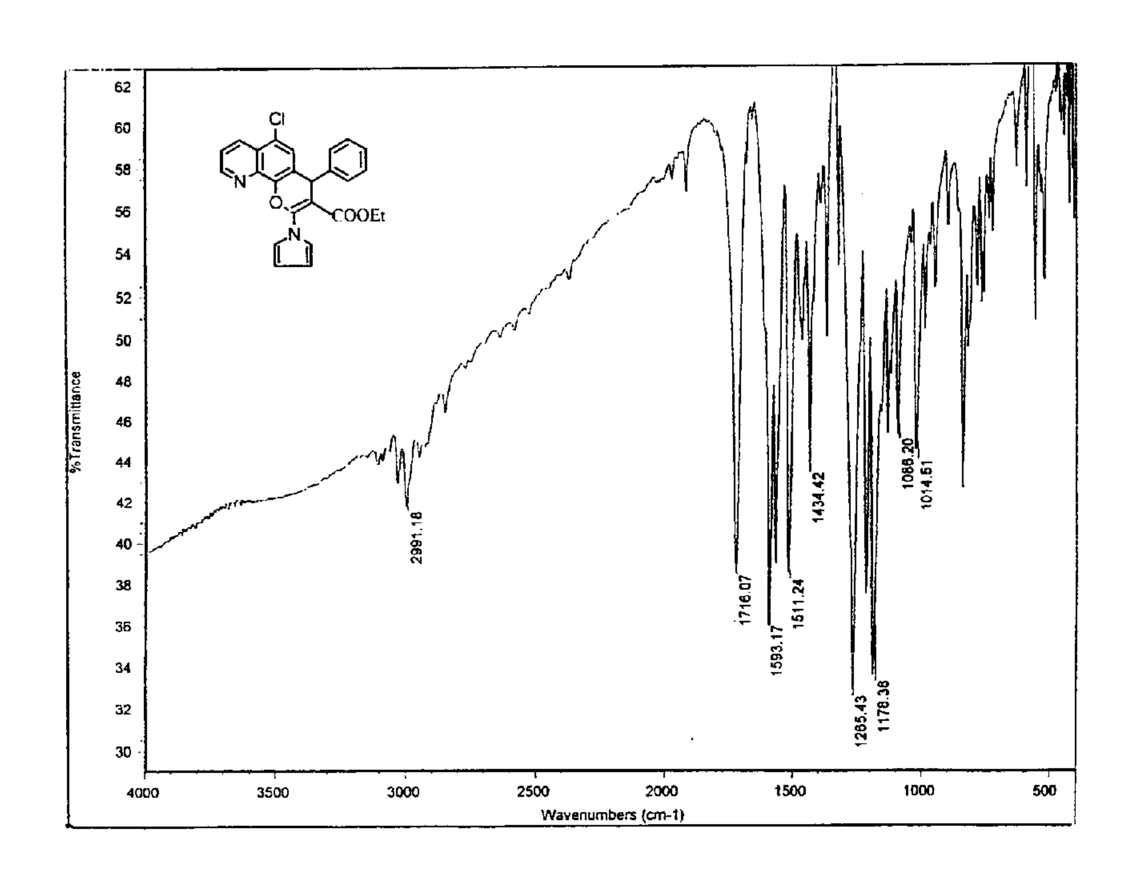


Fig.(90): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(238_a)**.

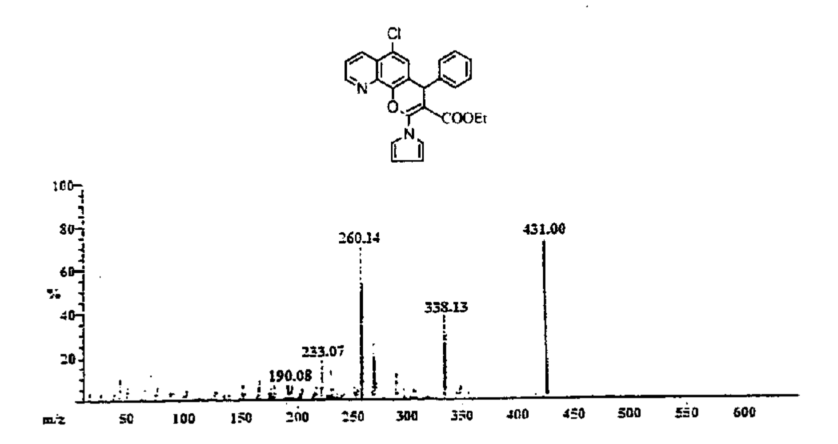


Fig.(91): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(238_a)**.

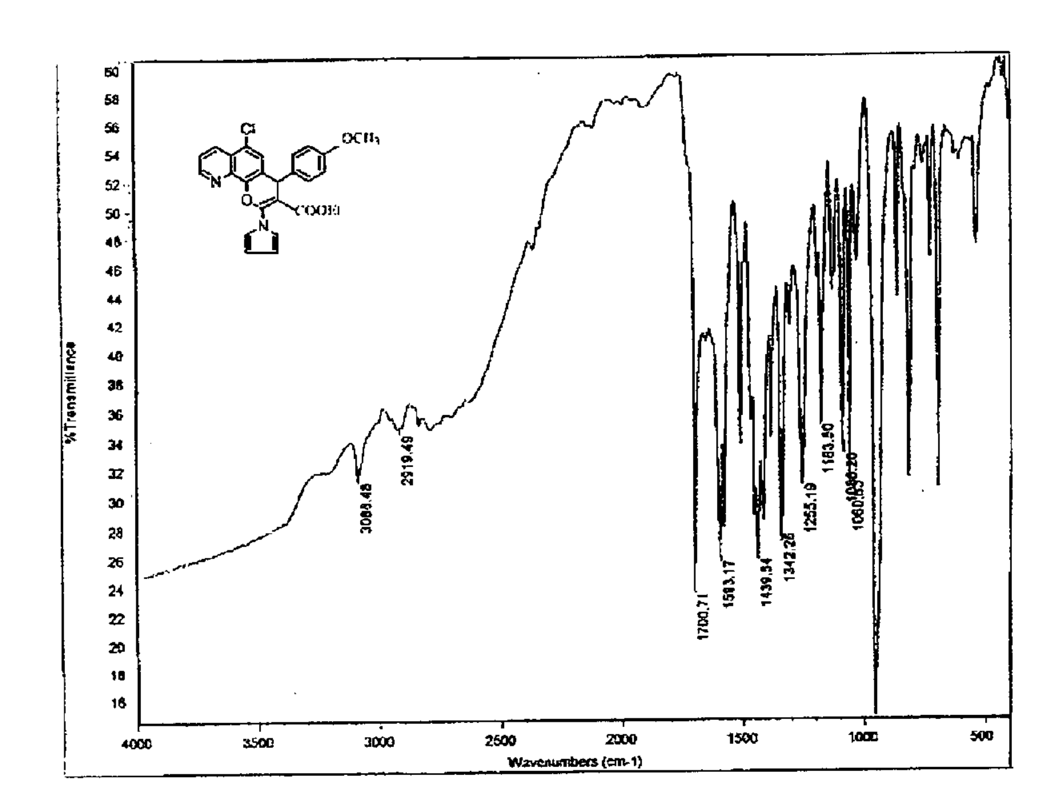


Fig.(92): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carboxylate **(238$_b$)**.

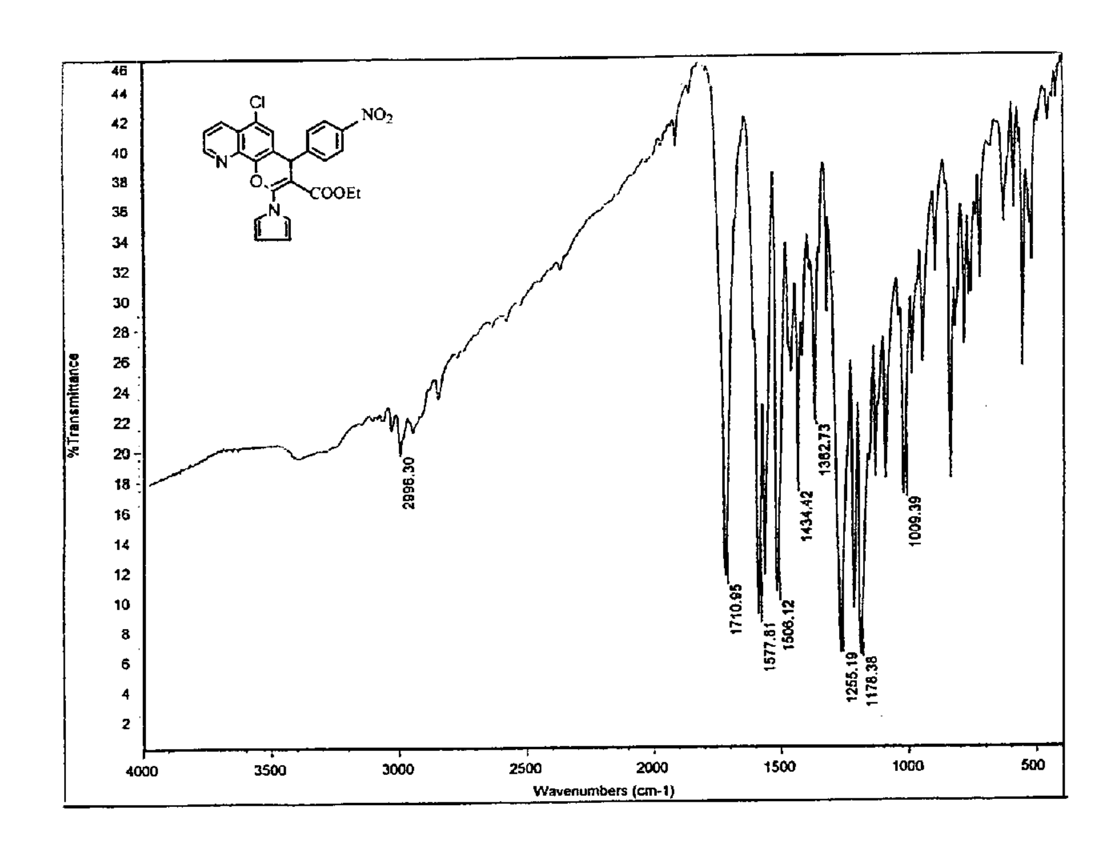


Fig.(93): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano[3,2-h]-quinoline-3-carboxylate **(238$_c$)**.

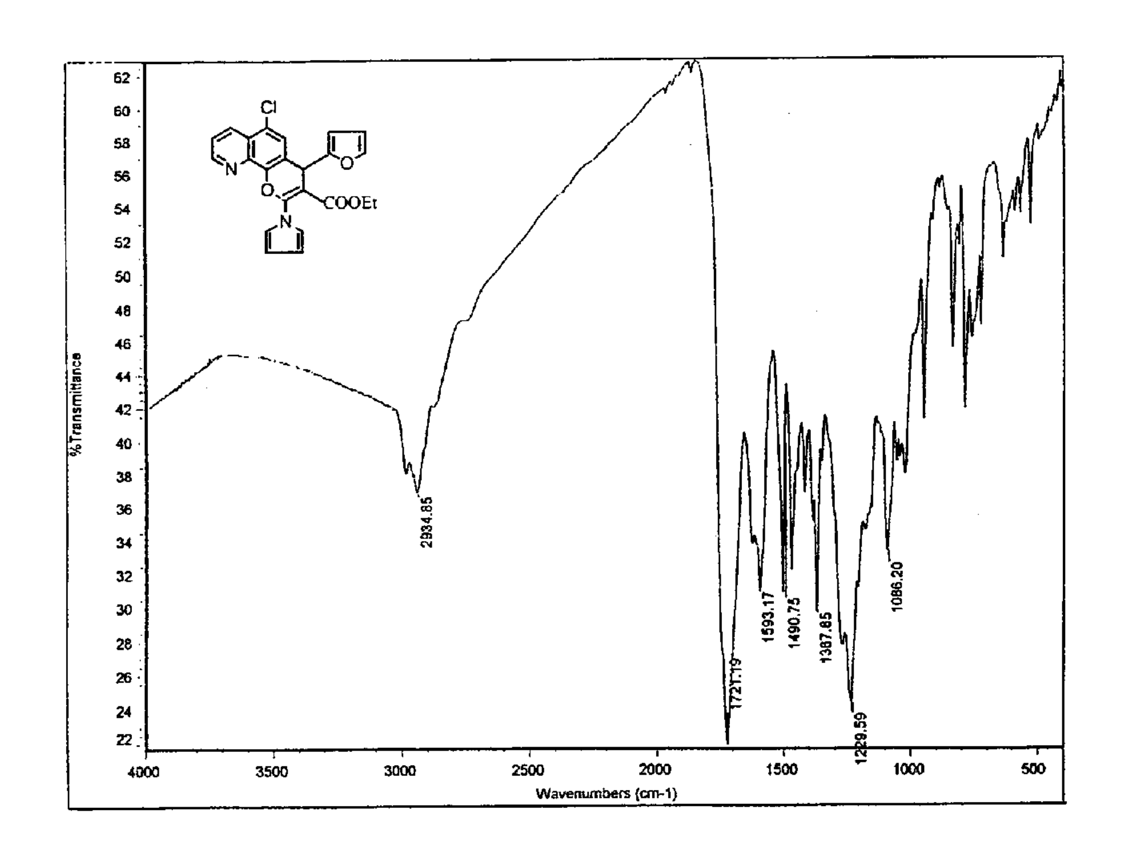


Fig.(94): Ethyl 2-(1-pyrrolyl)-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(238_d)**.

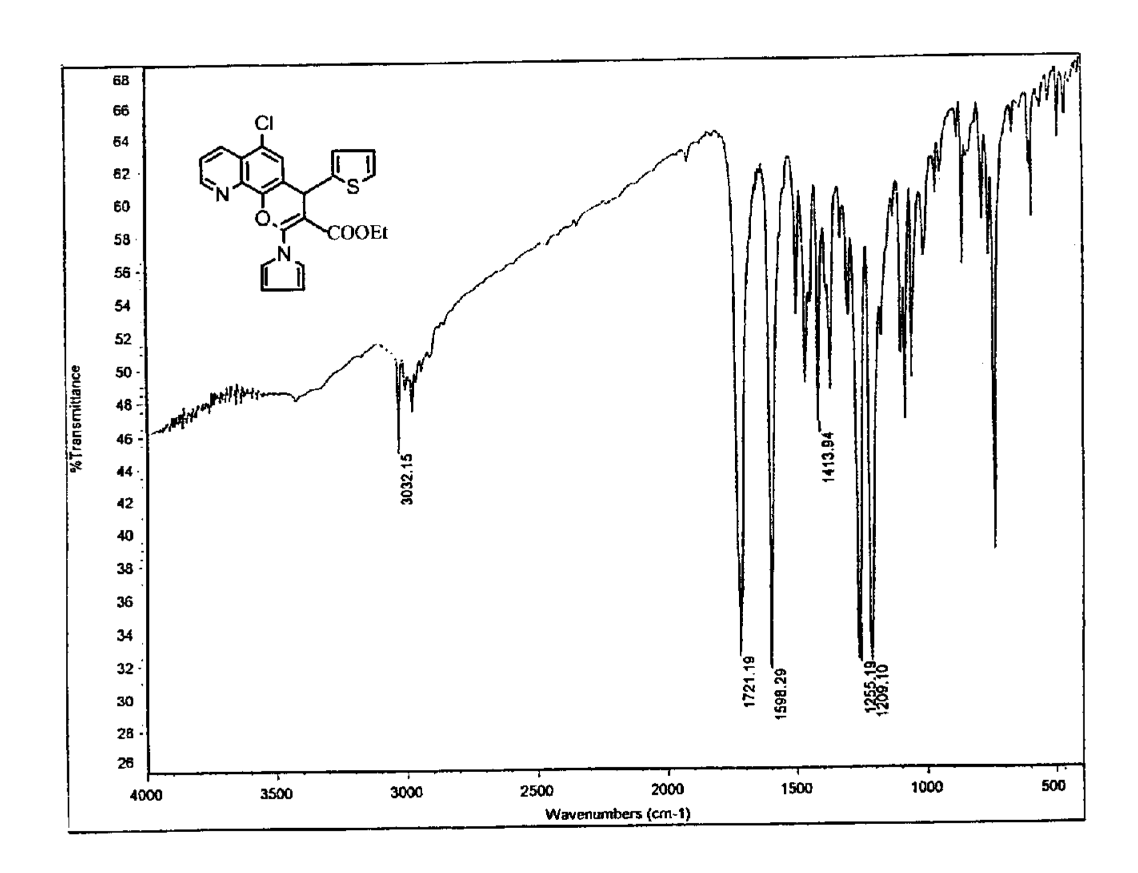


Fig.(95): Ethyl 2-(1-pyrrolyl)-6-chloro-4-thienyl-4H-pyrano[3,2-h]quinoline-3-carboxylate **(238$_e$)**.

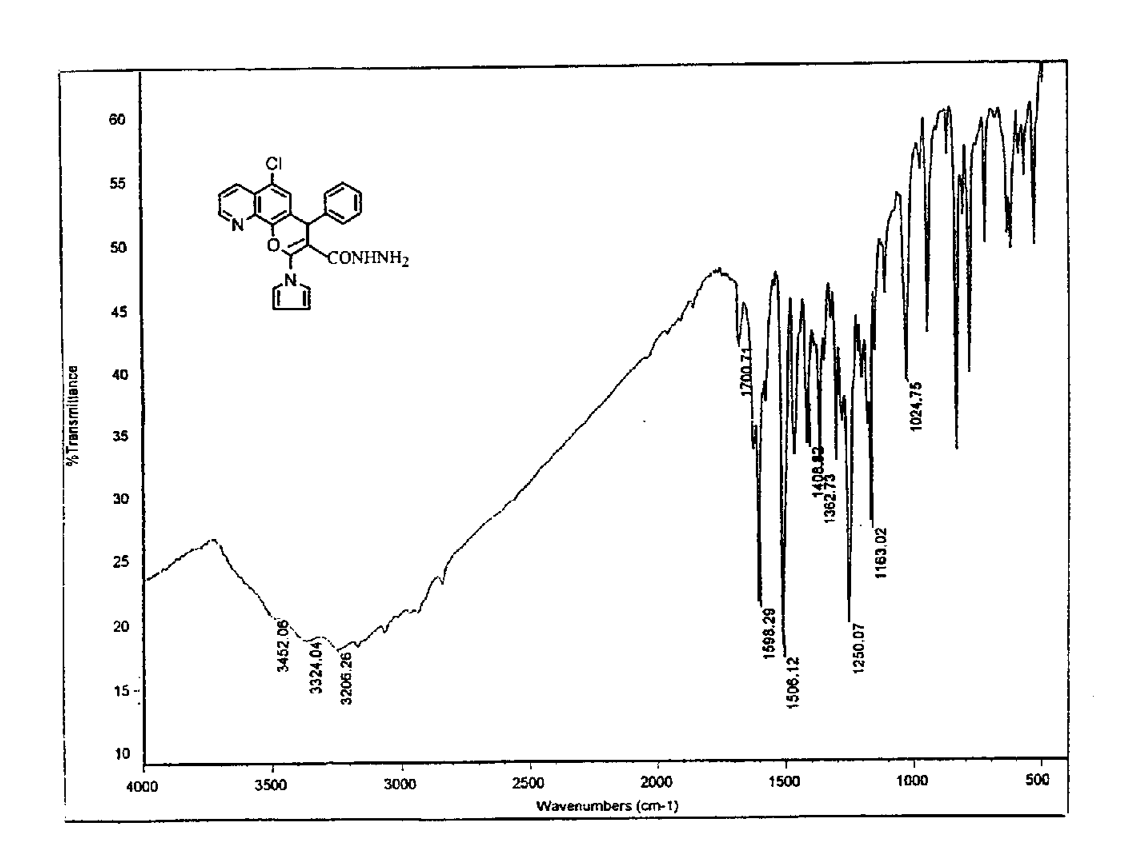
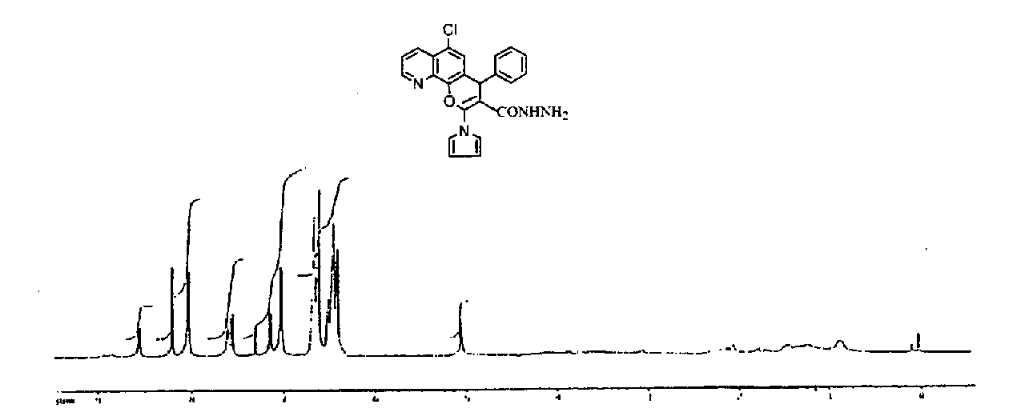


Fig.(96): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbohydrazide **(239_a)**.



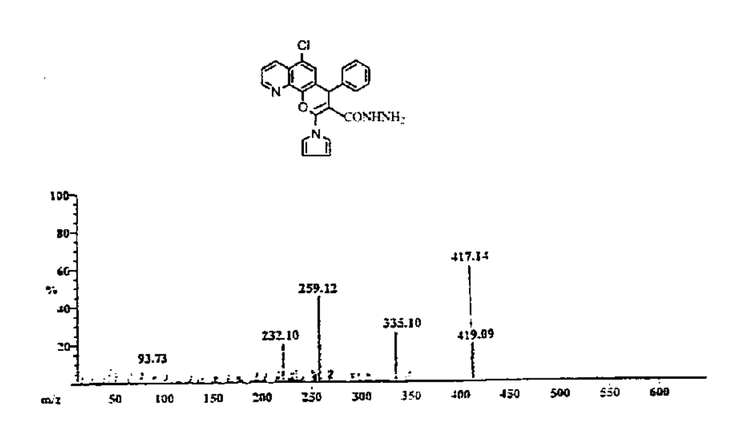


Fig.(97): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbohydrazide **(239$_a$)**.

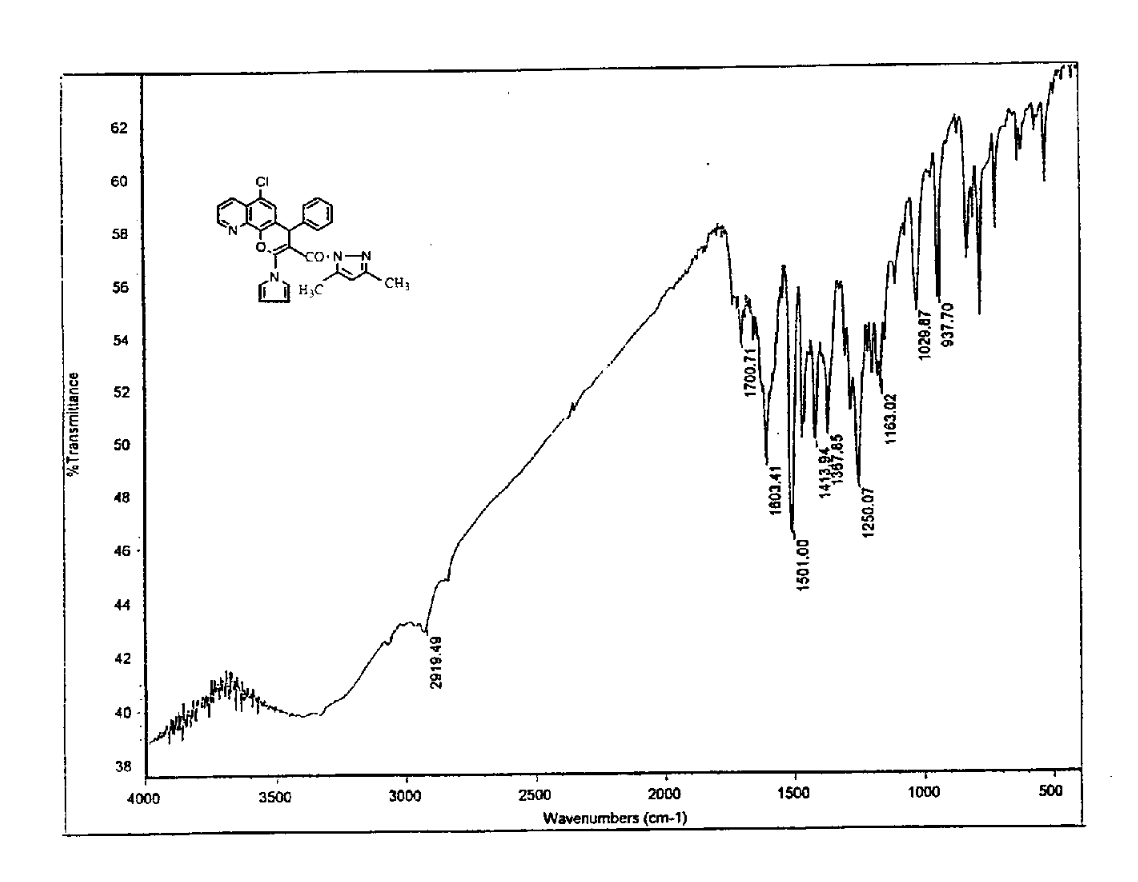
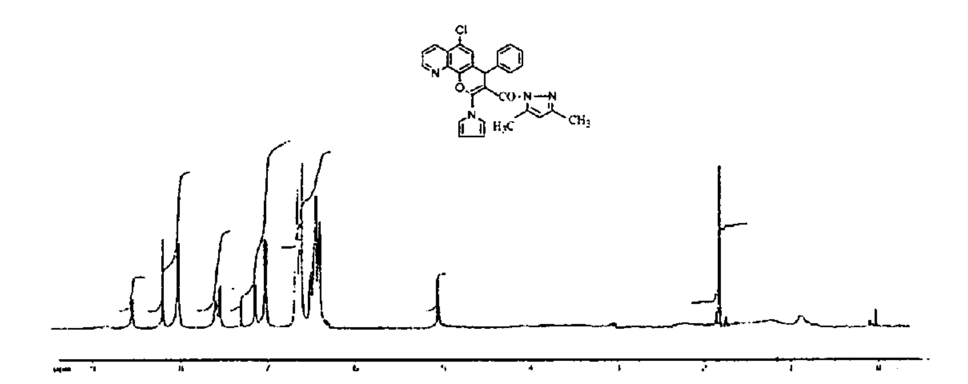


Fig.(98): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-phenyl-4H-pyrano[3,2-h]quinoline **(240_a)**.



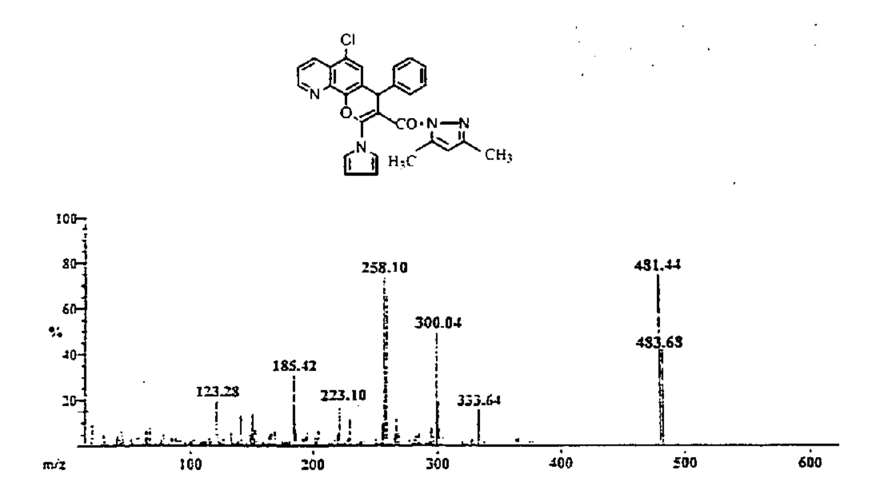


Fig.(99): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-phenyl-4H-pyrano[3,2-h]quinoline **(240_a)**.

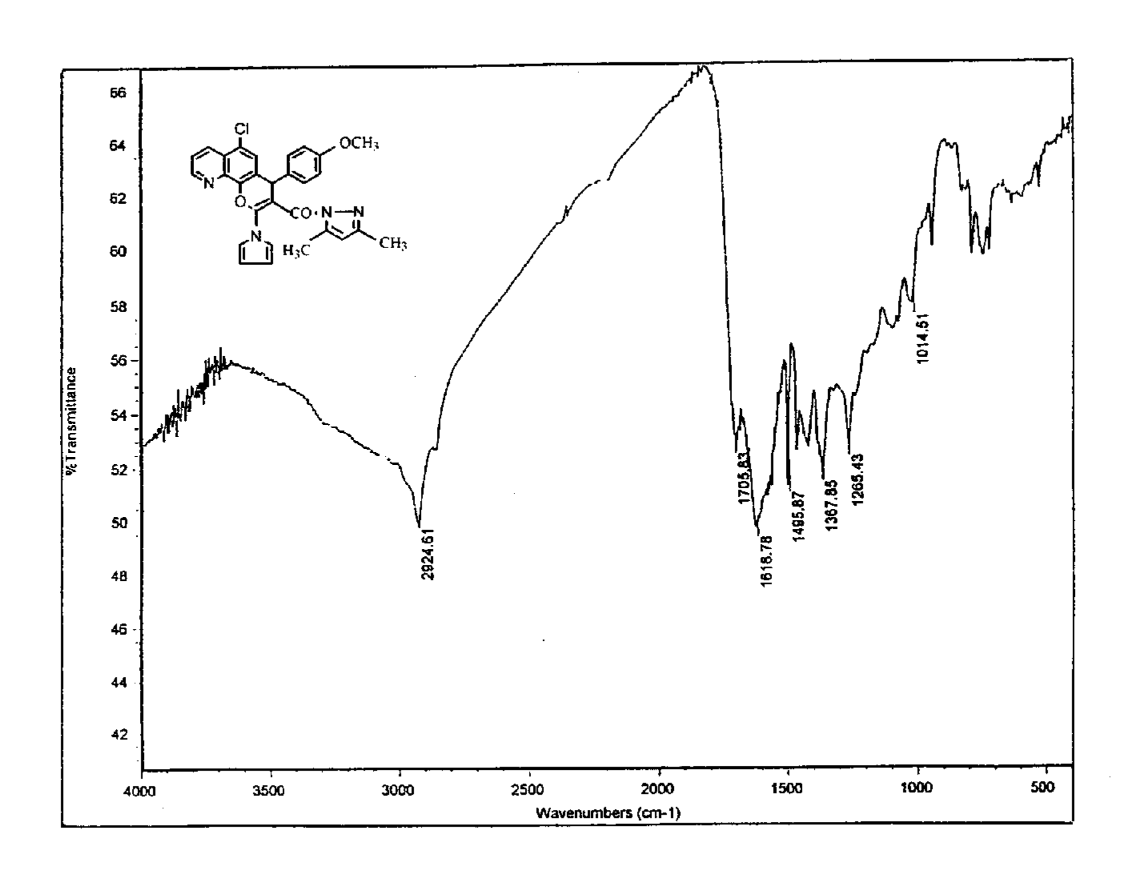
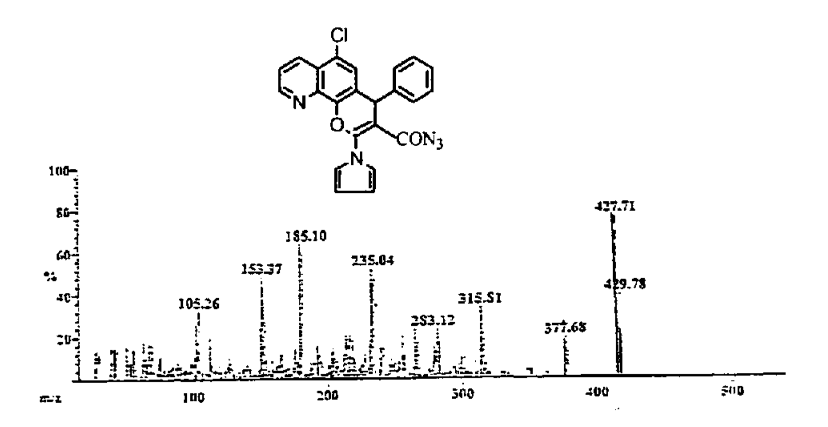


Fig.(100): 6-Chloro-2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-(4-methoxy)phenyl-4H-pyrano[3,2-h]quinoline **(240_b)**.



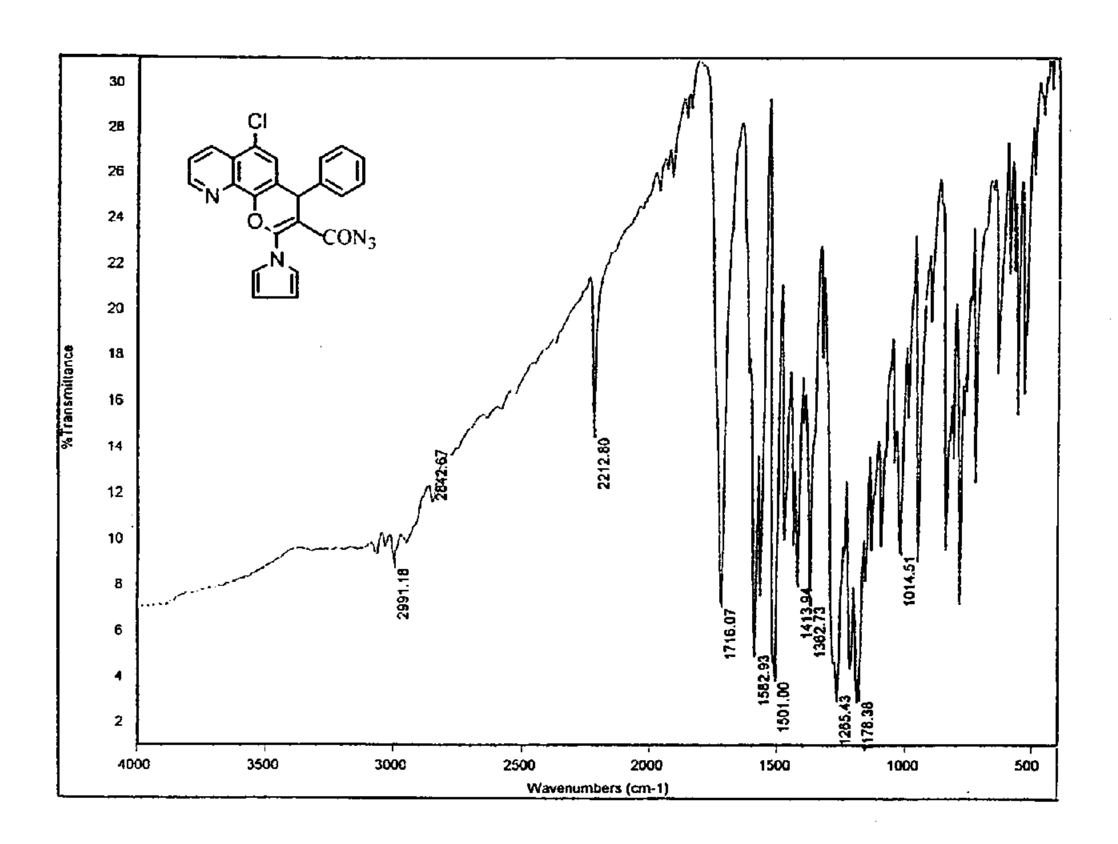


Fig.(101): 6-Chloro-2-(1-pyrrolyl)-4-phenyl-4H-pyrano[3,2-h]quinolin-3-oylazide **(241_a)**.

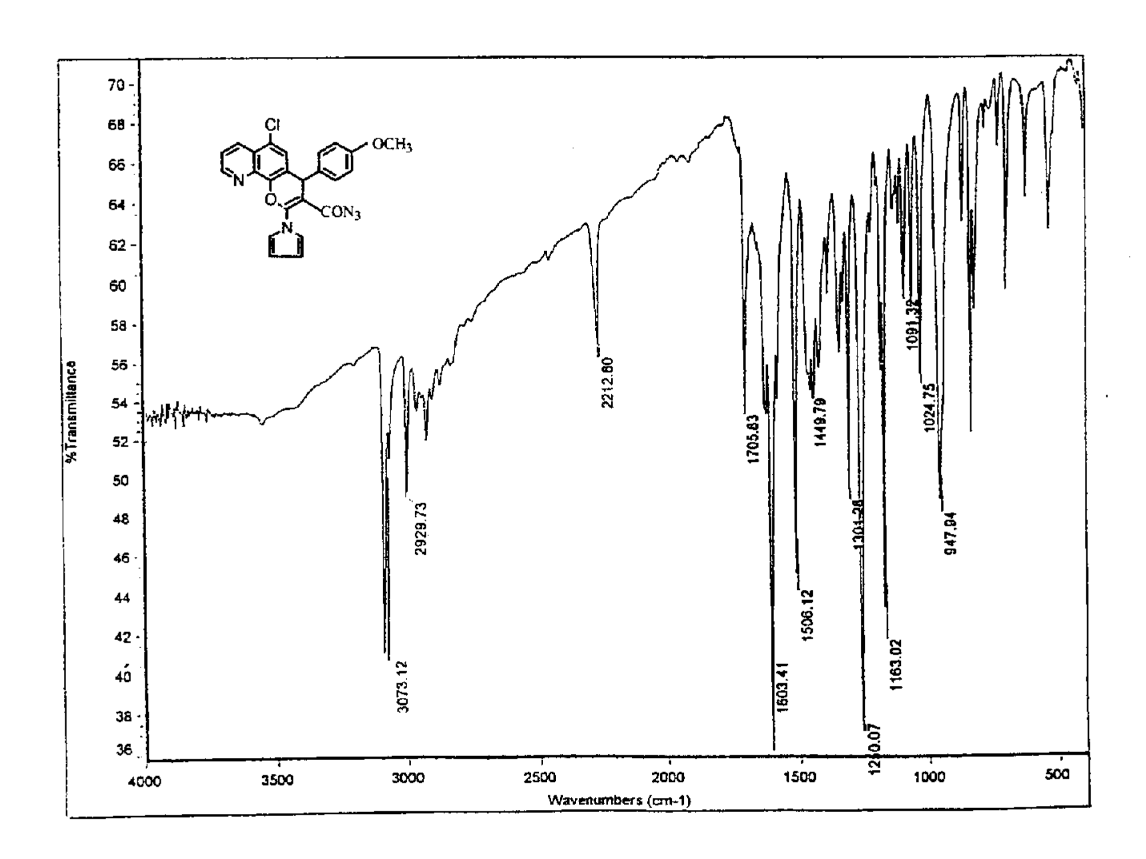


Fig.(102): 6-Chloro-2-(1-pyrrolyl)-4-(4-methoxy)phenyl-4H-pyrano[3,2-h]-quinolin-3-oylazide **(241$_b$)**.

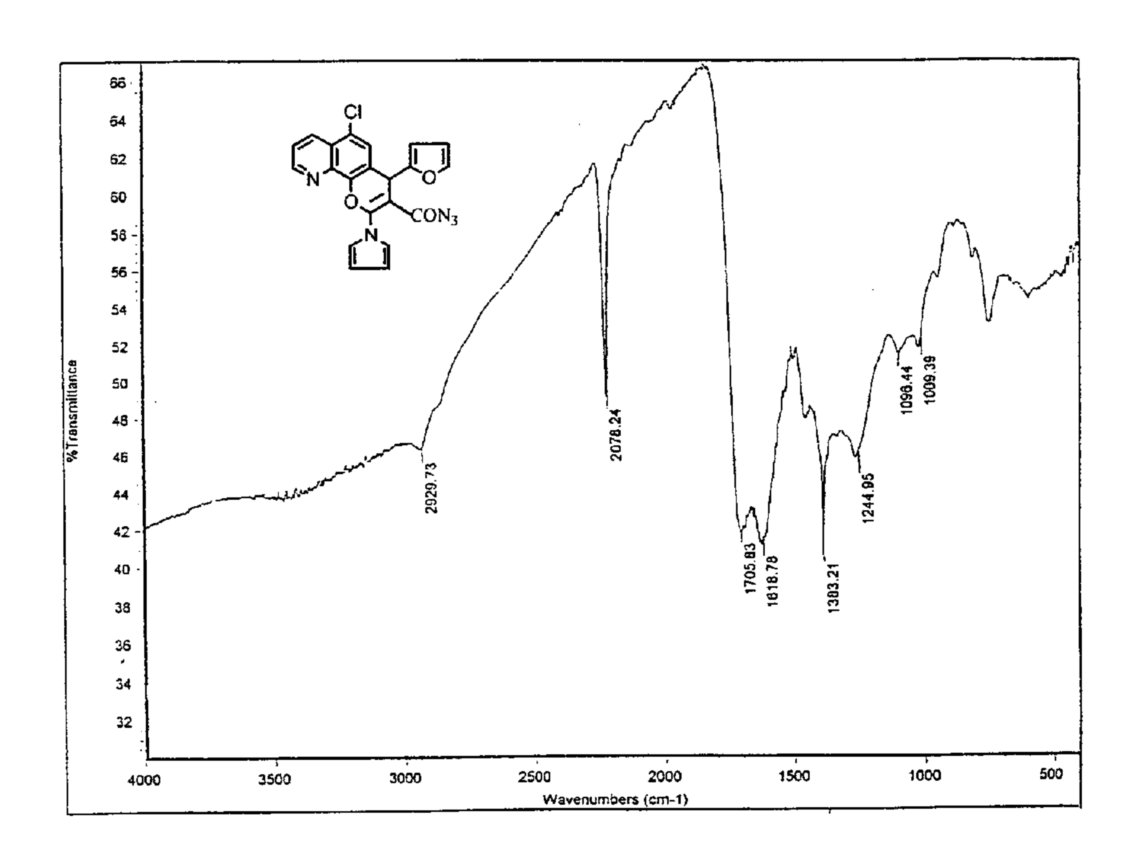


Fig.(103): 6-Chloro-2-(1-pyrrolyl)-4-furyl-4H-pyrano[3,2-h]quinolin-3-oylazide (**241_d**).

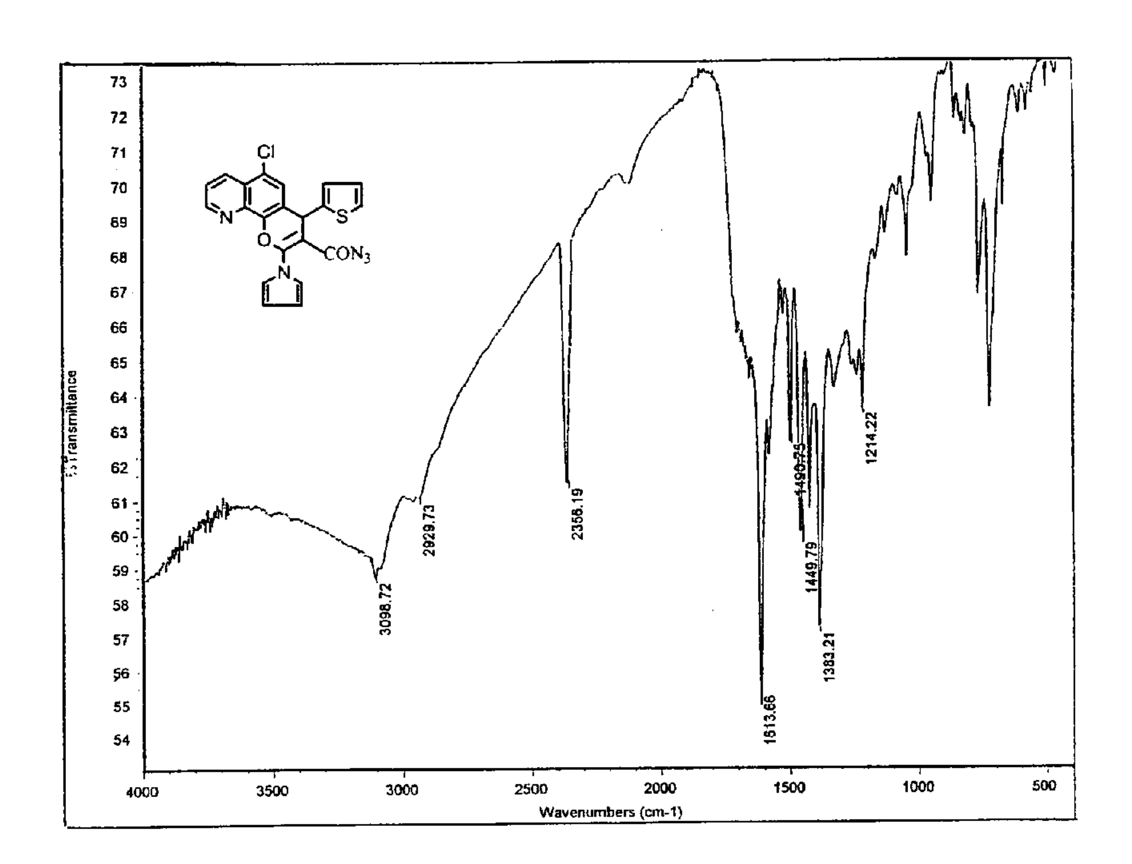


Fig.(104): 6-Chloro-2-(1-pyrrolyl)-4-thienyl-4H-pyrano[3,2-h]quinolin-3-oylazide (**241_e**).

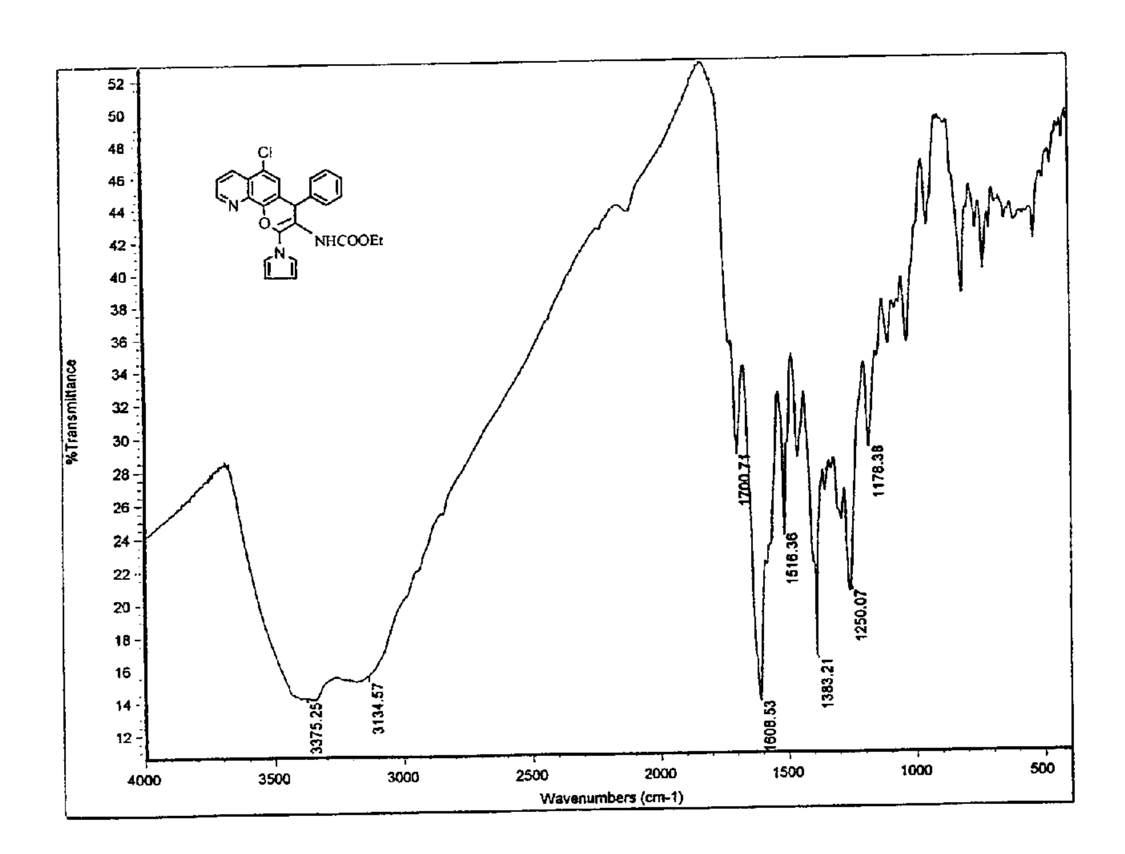
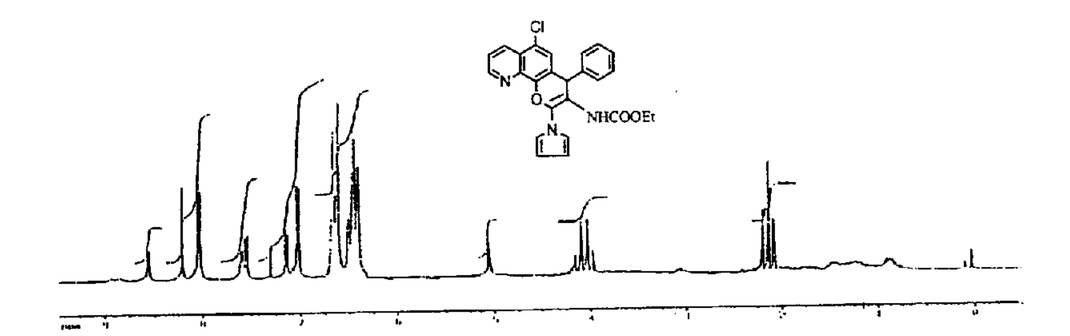


Fig.(105): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbamate **(242_a)**.



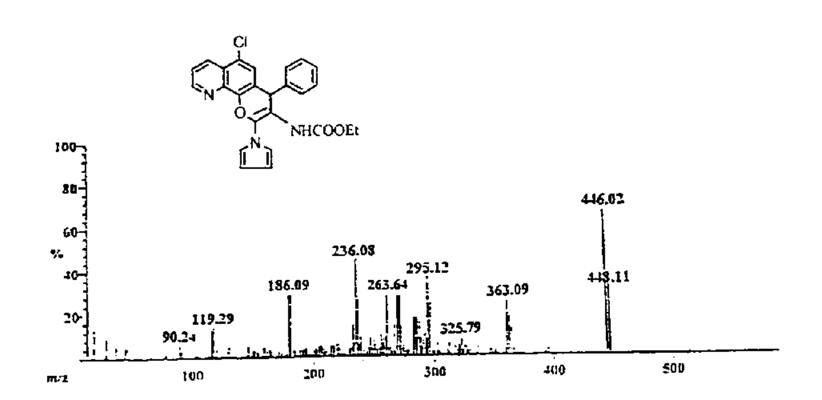


Fig.(106): Ethyl 2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbamate (**242_a**).

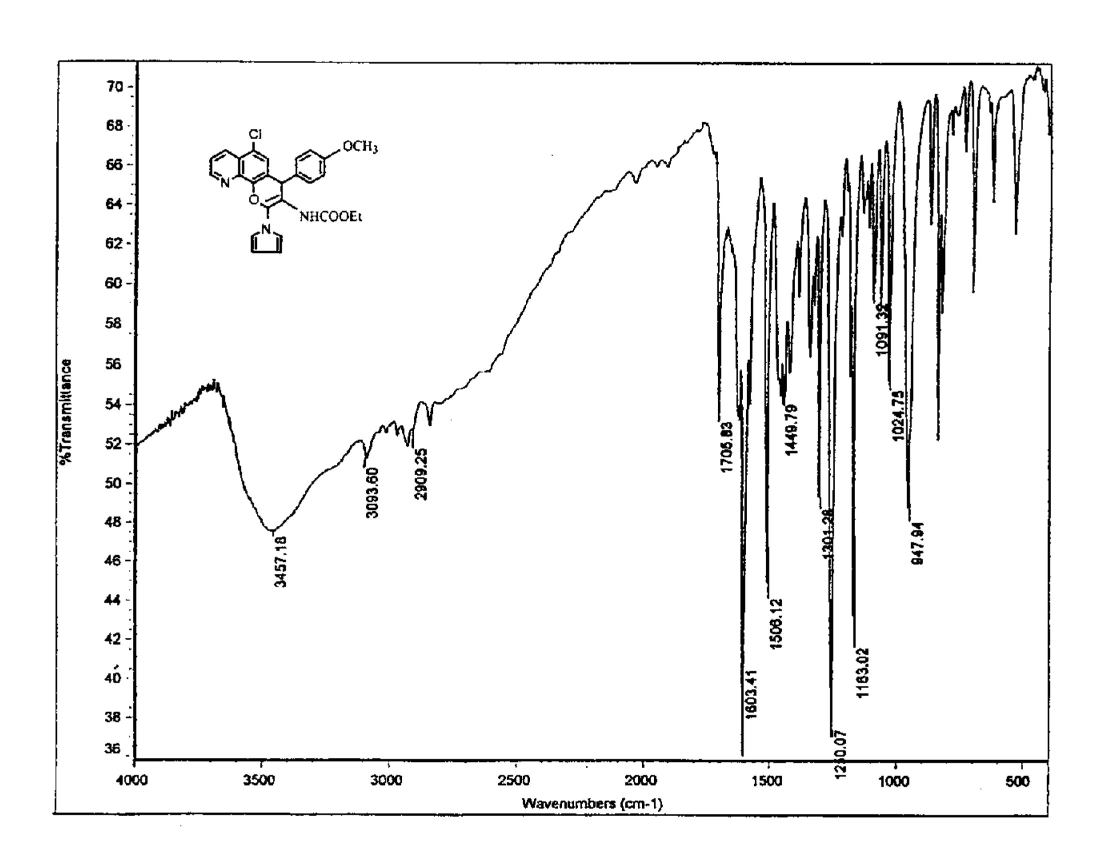


Fig.(107): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinoline-3-carbamate **(242_b)**.

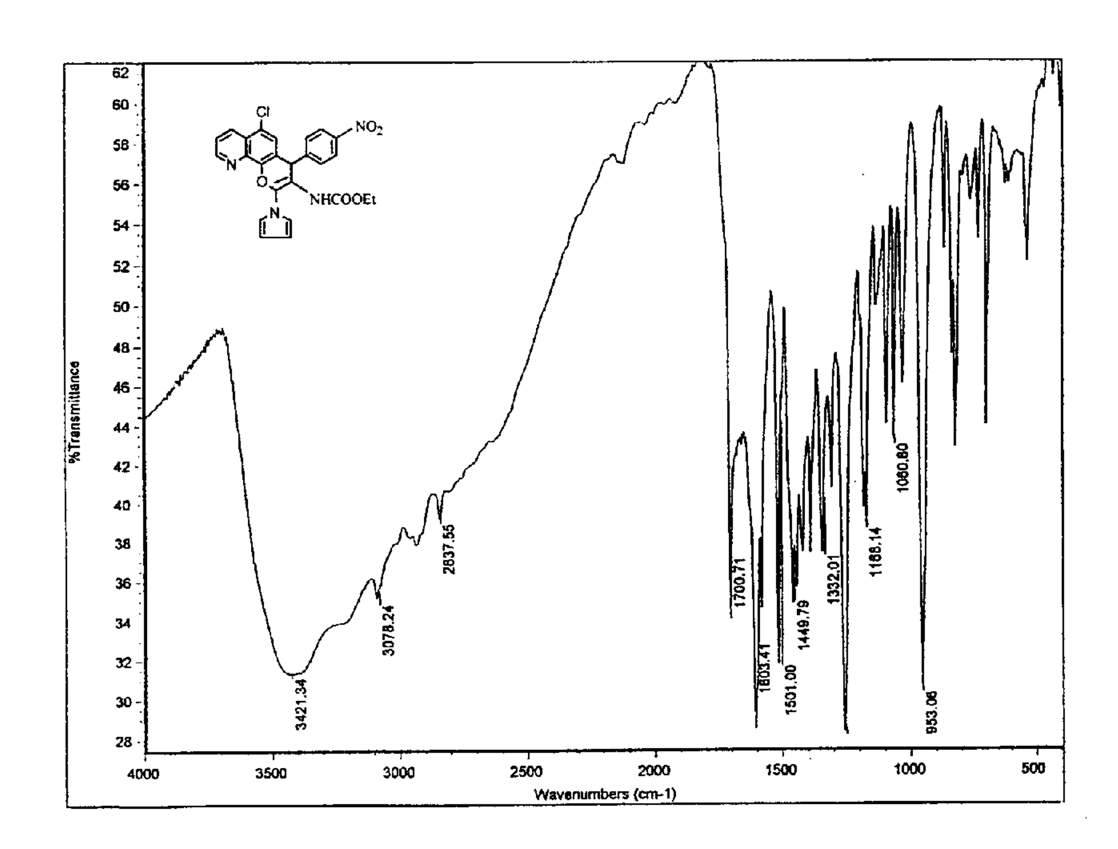


Fig.(108): Ethyl 2-(1-pyrrolyl)-6-chloro-4-(4-nitro)phenyl-4H-pyrano-[3,2-h]quinoline-3-carbamate (**242$_c$**).

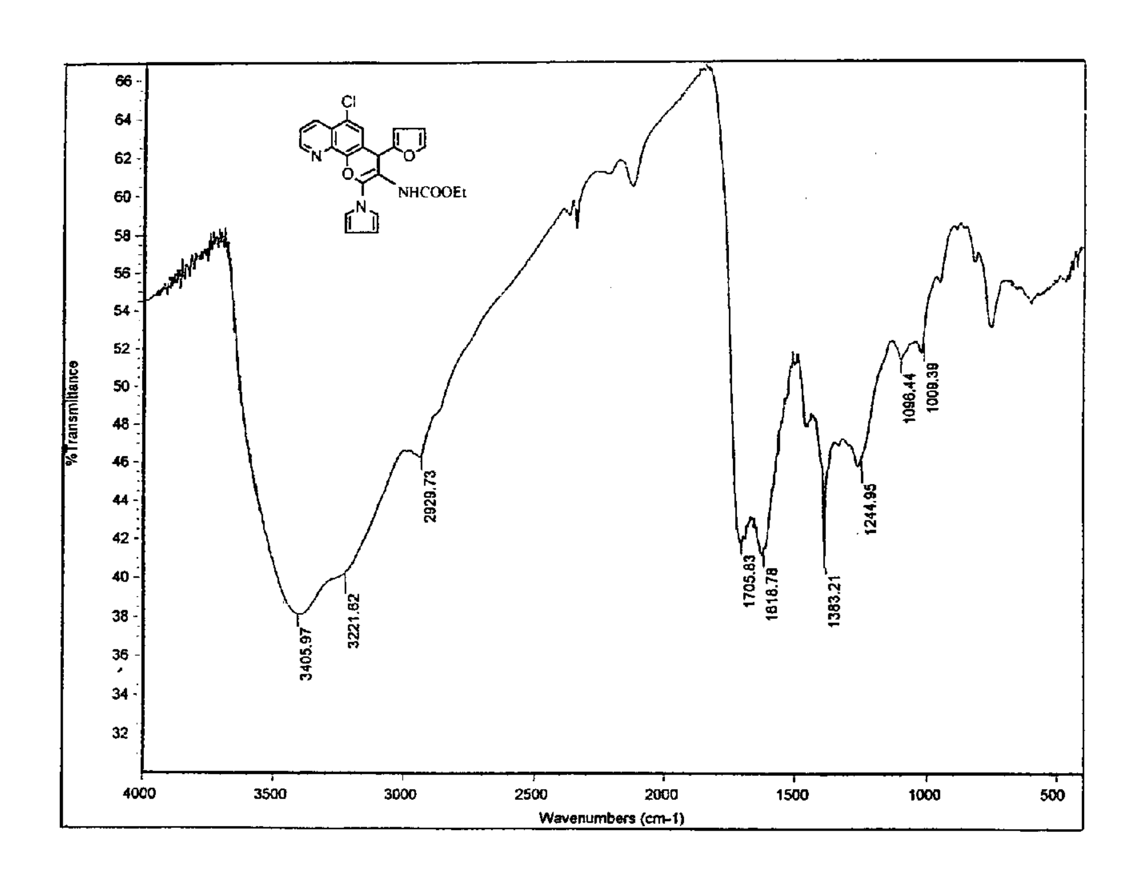
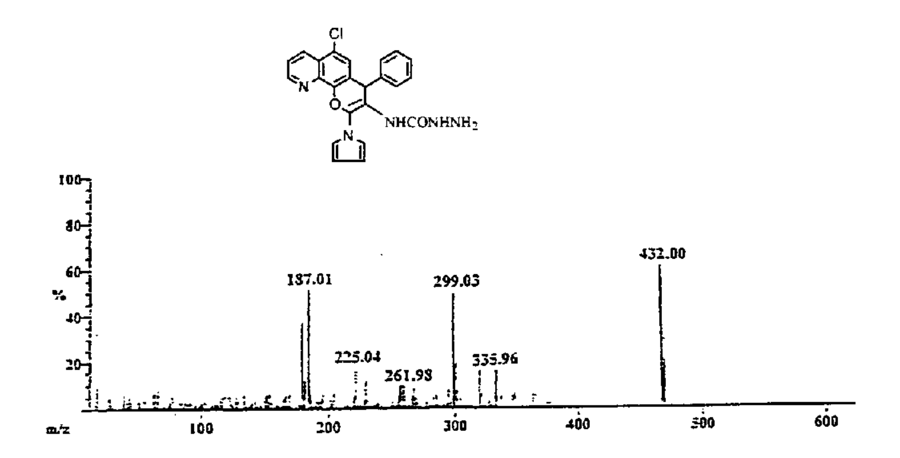


Fig.(109): Ethyl 2-(1-pyrrolyl)-6-chloro-4-furyl-4H-pyrano[3,2-h]quinoline-3-carbamate **(242_d)**.



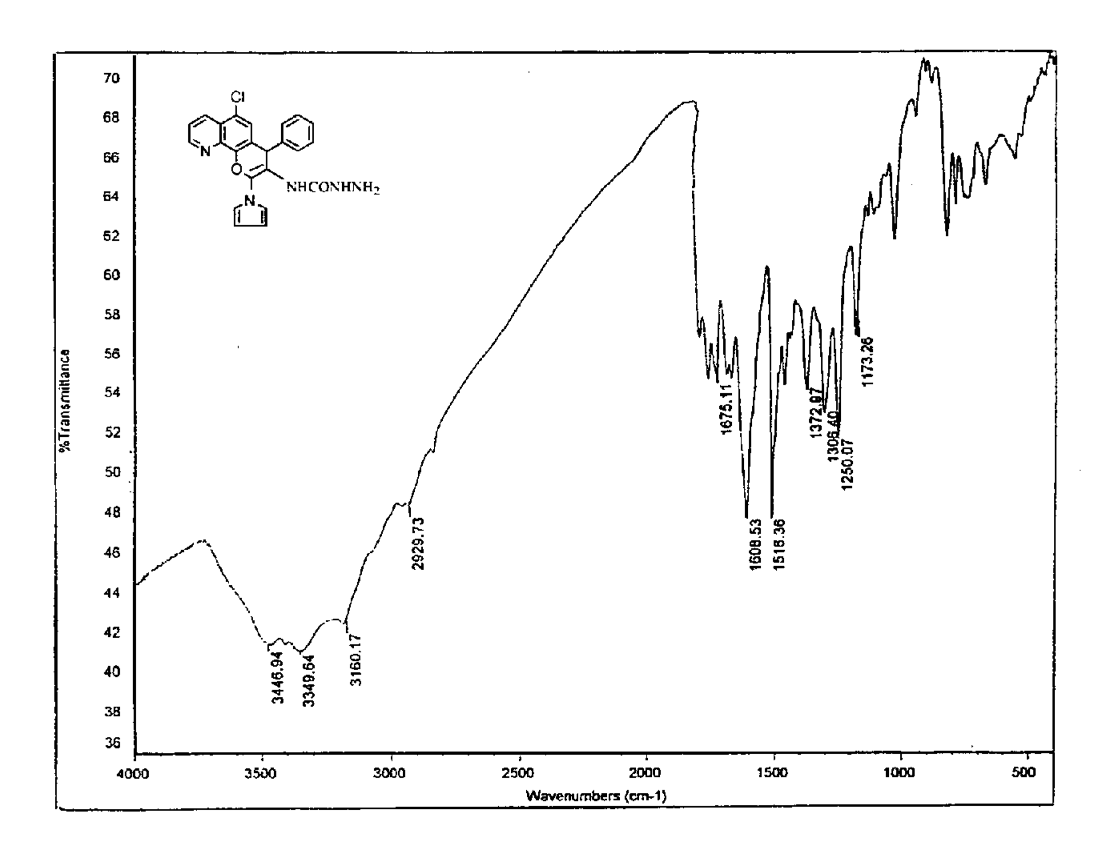


Fig.(110): 4-[2-(1-pyrrolyl)-6-chloro-4-phenyl-4H-pyrano[3,2-h]quinolin-3-yl]-semicarbazide (**243_a**).

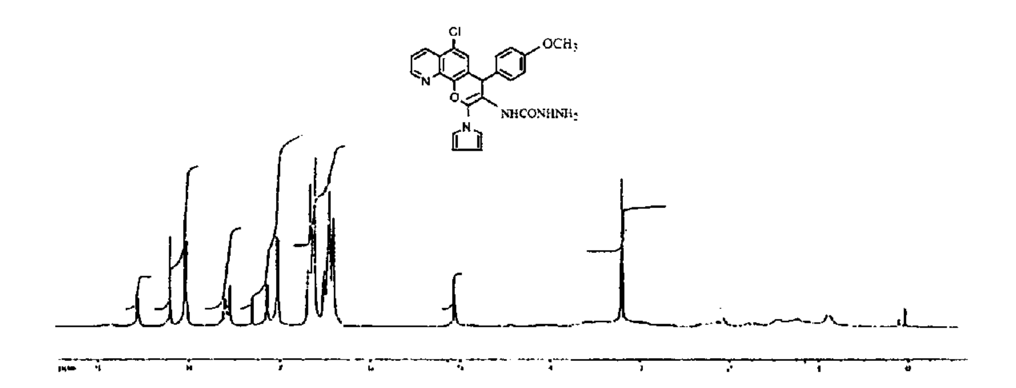
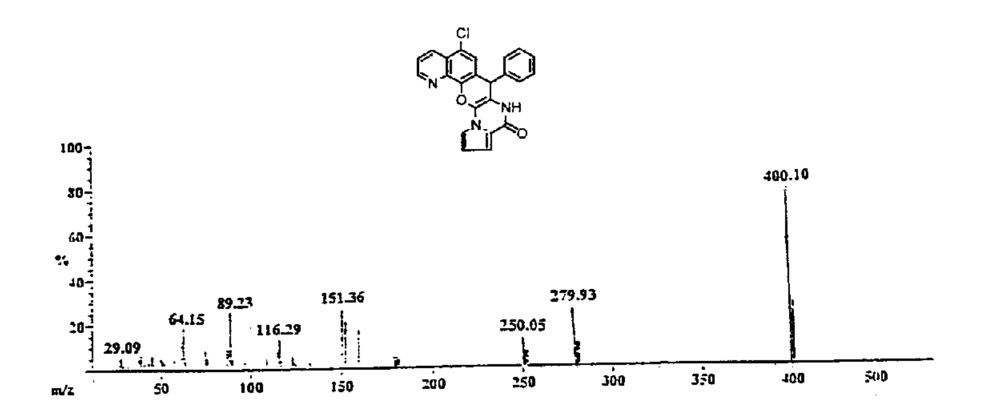


Fig.(111): 4-[2-(1-pyrrolyl)-6-chloro-4-(4-methoxy)phenyl-4H-pyrano-[3,2-h]quinolin-3-yl]semicarbazide **(243_b)**.



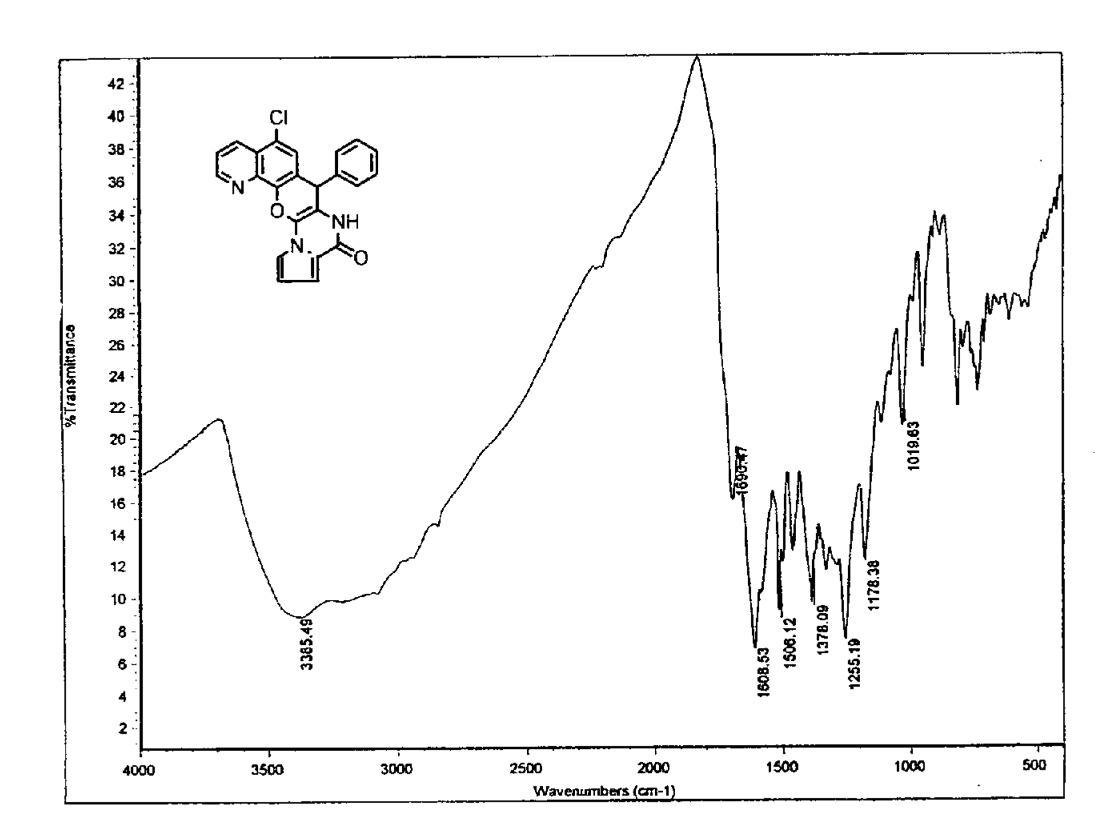


Fig.(112): 5-Chloro-7-phenyl-9-oxo-7,8-dihydropyrrolo[1",2":1',2']pyrazino-[5',6':5,6]pyrano[3,2-h]quinoline (**244_a**).

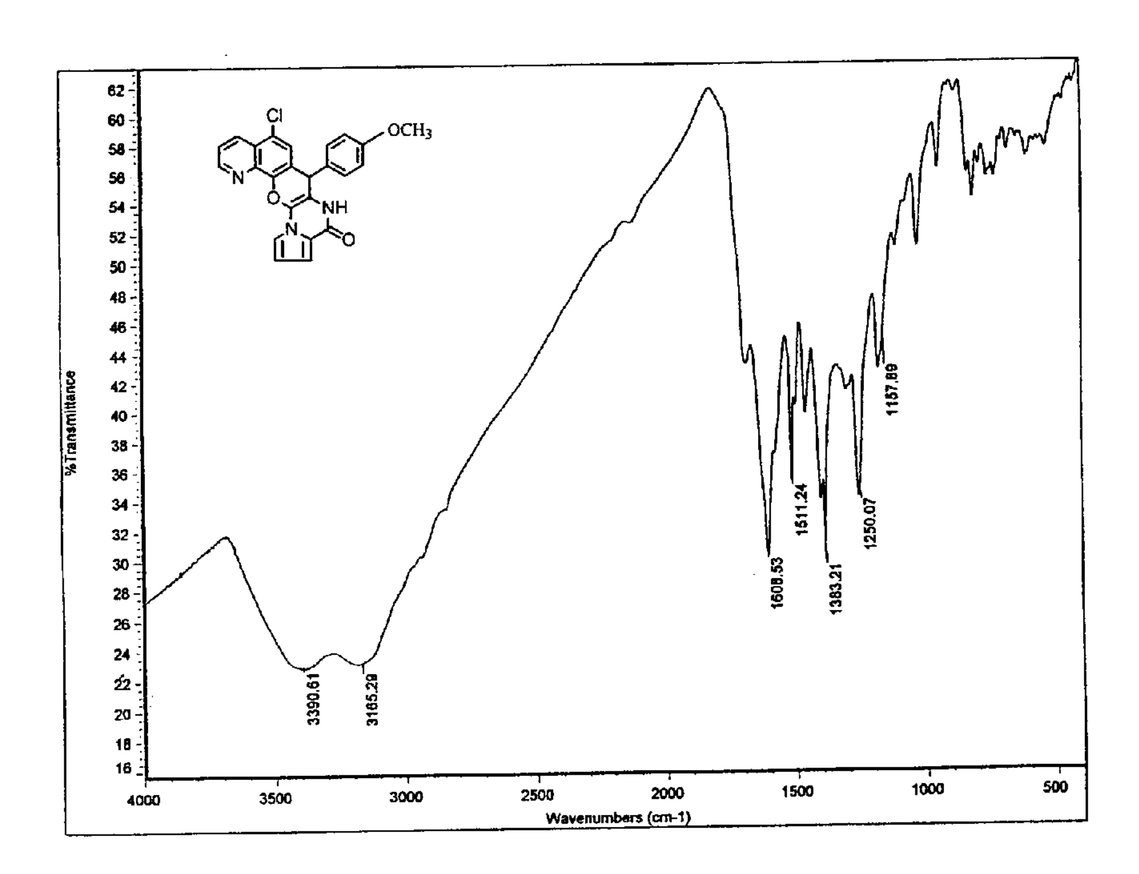


Fig.(113): 5-Chloro-7-(4-methoxy)phenyl-9-oxo-7,8-dihydropyrrolo[1'',2'':1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(244$_b$)**.

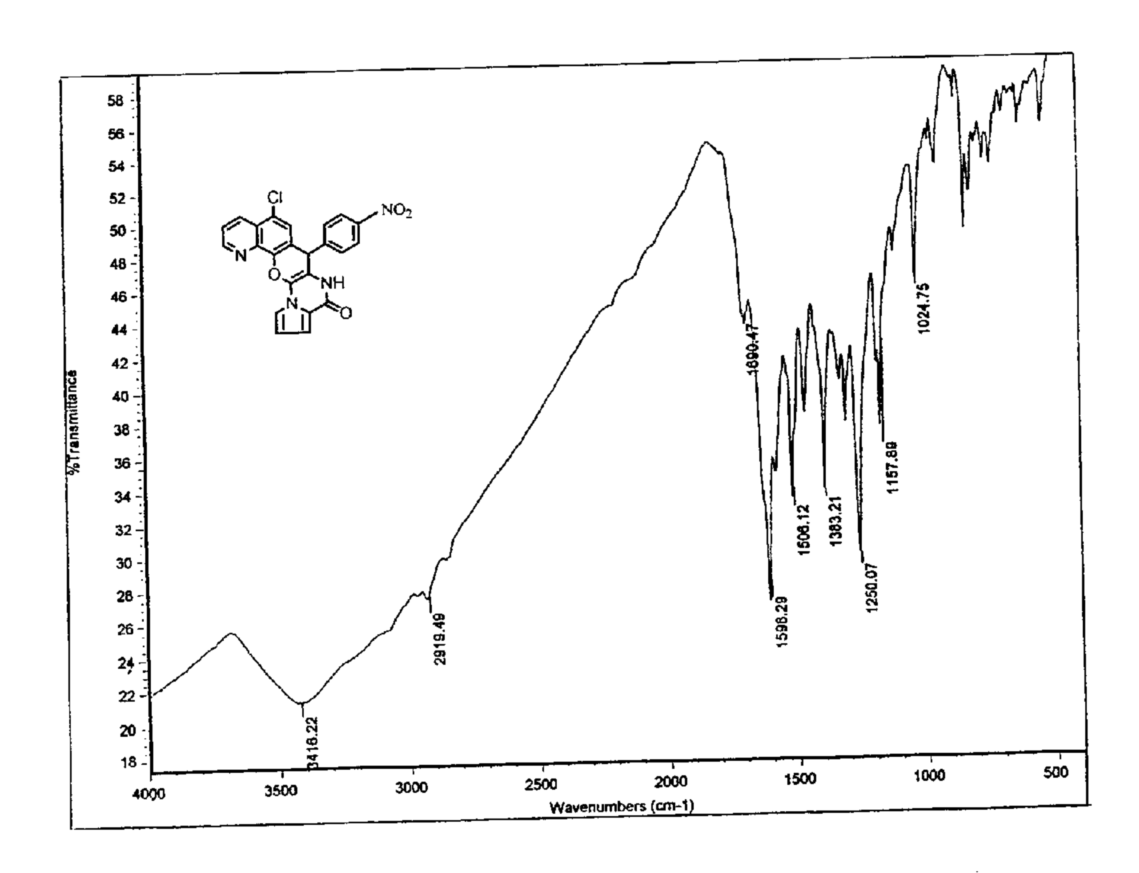


Fig.(114): 5-Chloro-7-(4-nitro)phenyl-9-oxo-7,8-dihydropyrrolo[1",2":1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(244$_c$)**.

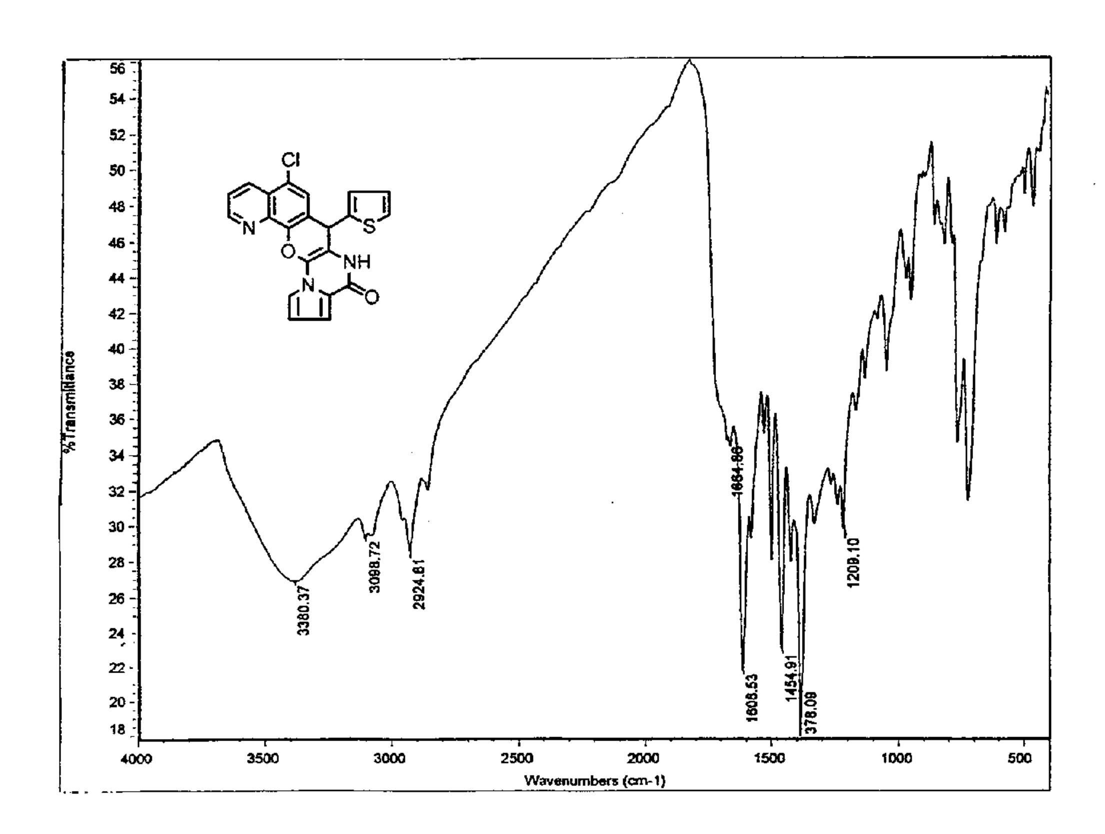
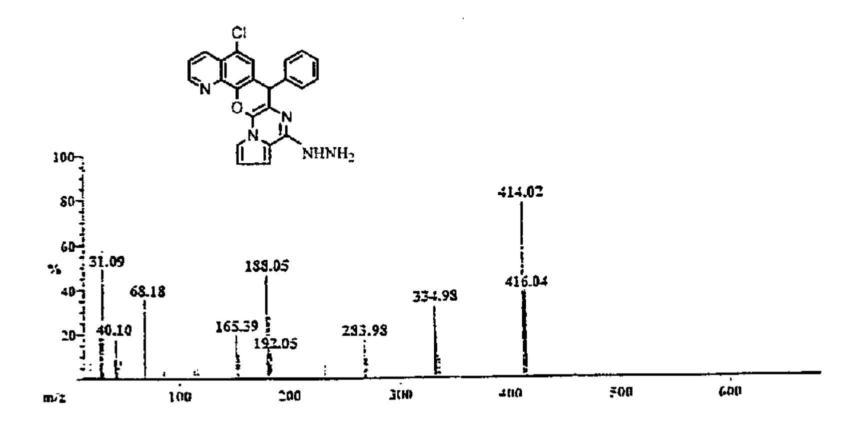


Fig.(116): 5-Chloro-7-thienyl-9-oxo-7,8-dihydropyrrolo[1",2":1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline (**244$_e$**).



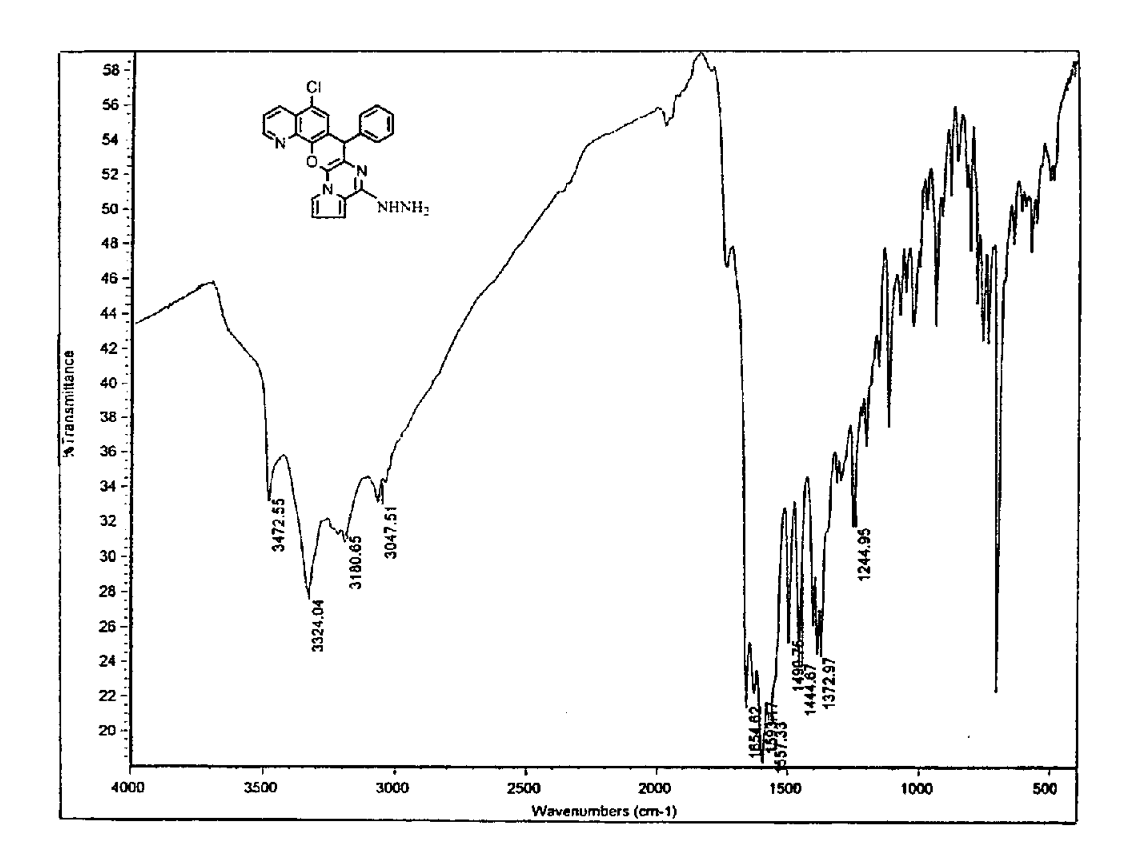


Fig.(117): 5-Chloro-9-hydrazino-7-phenyl-7H-pyrrolo[1",2":1',2']-pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(246_a)**.

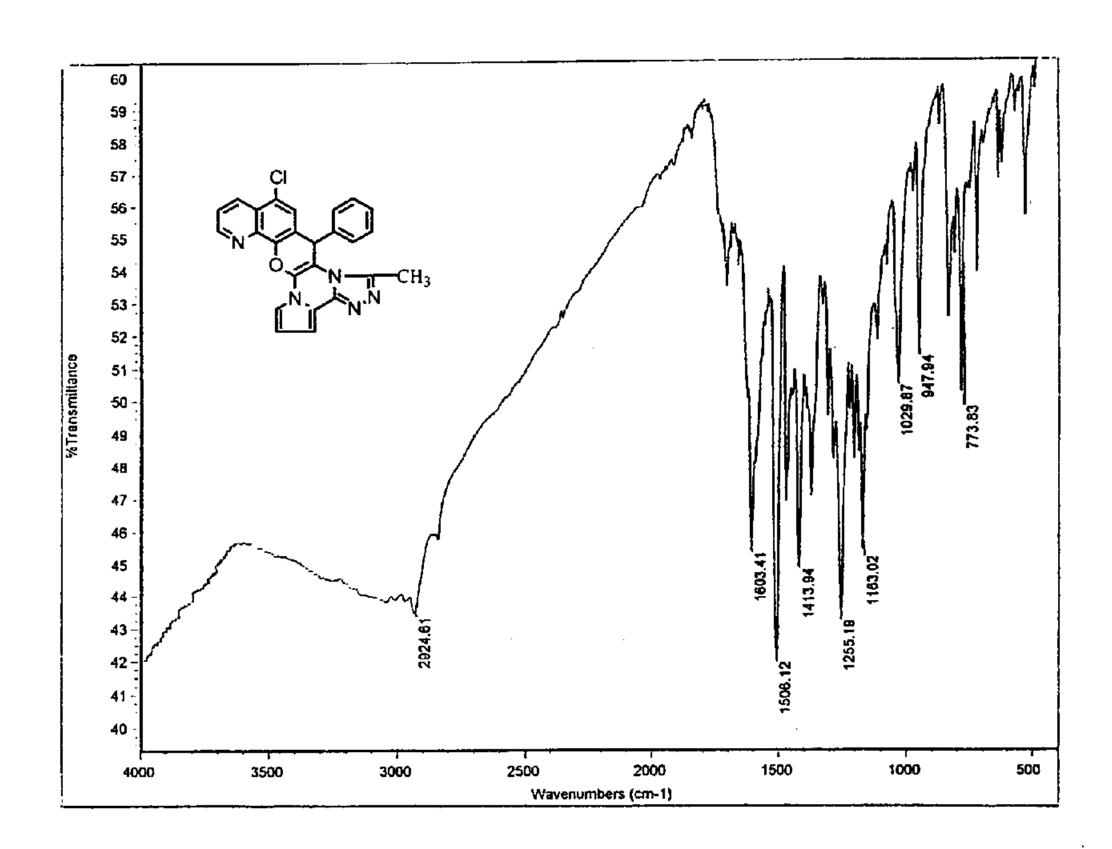


Fig.(118): 5-Chloro-9-methyl-7-phenyl-7H-1,2,4-triazolo[3",4":3',4']-pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(247_a)**.

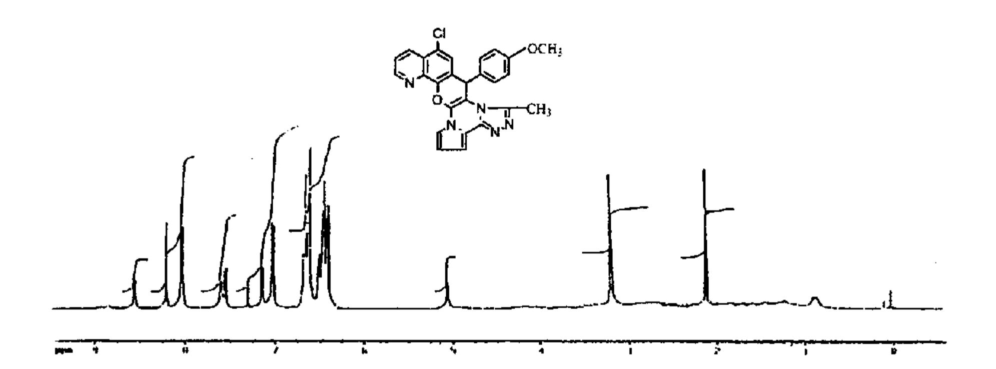
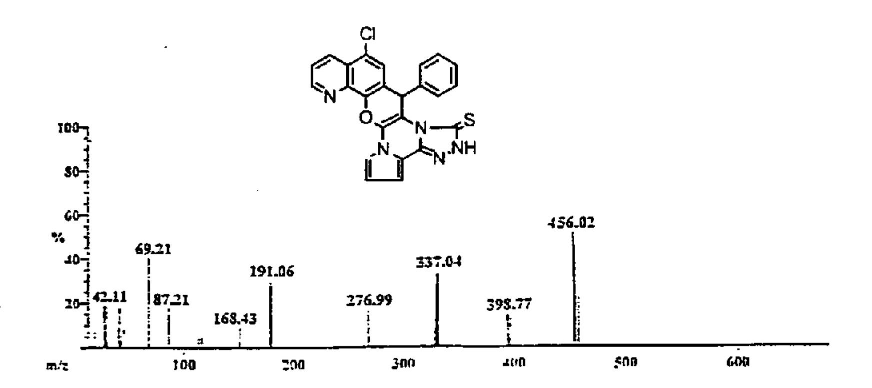


Fig.(119): 5-Chloro-9-methyl-7-(4-methoxy)phenyl-7H-1,2,4-triazolo-[3",4":3',4']pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(247_b)**.



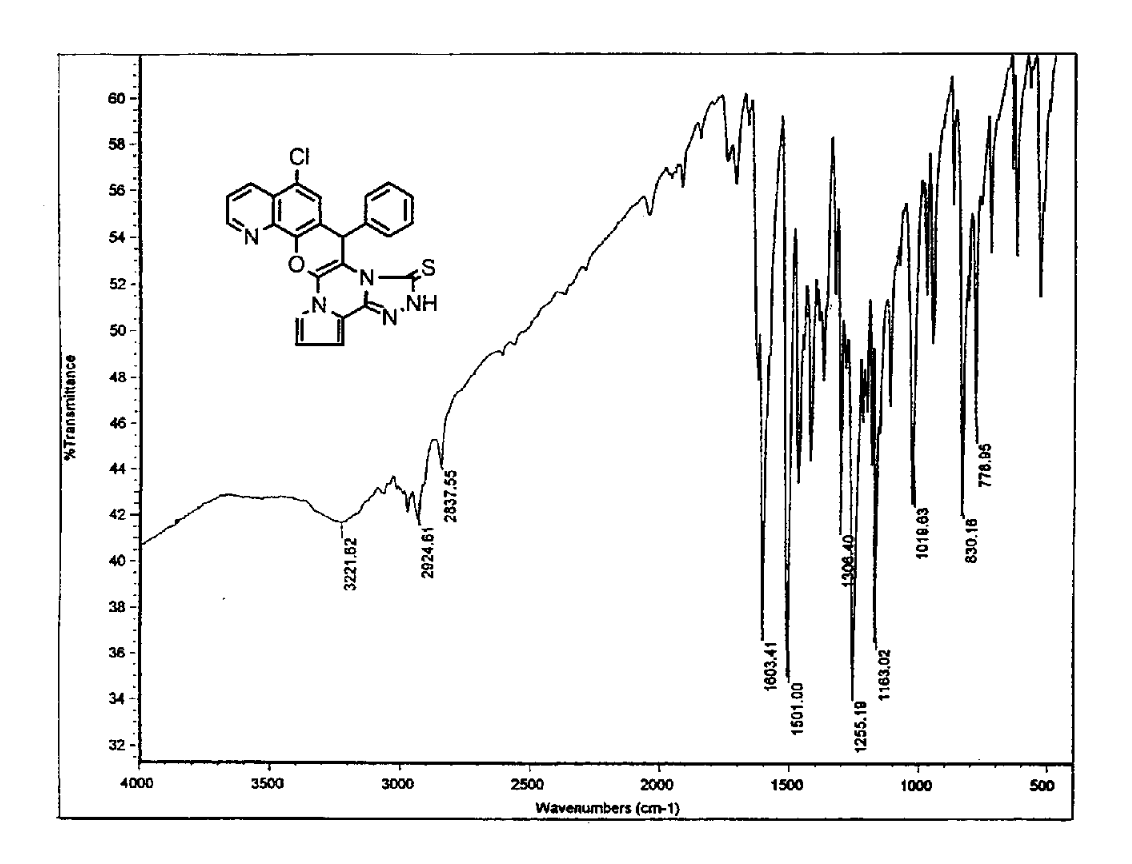


Fig.(120): 5-Chloro-7-phenyl-9-thioxo-7,10-dihydro-1,2,4-triazolo[3",4":3',4']-pyrrolo[1",2":1',2']pyrazino[5',6':5,6]pyrano[3,2-h]quinoline **(248_a)**.

Arabic Summary

الملخص العربي

تعتبر مركبات البيران و البيريميدين و الكينولين و الاميدازول و الترايازول و الترياــزين و البيرول و الديازين ذات نشاط بيولوجي فعال. فمركبات البيران تستخدم كمضادات للبكتيريا و الفطريات و الأورام و التوتر و الكينولين كمضادات للملا ريا و البكتريا و الفطريات و الربو و القرح و تصلب الشرايين و كمبيدات للأعشاب. و البيريميــدين كمضــادات للبكتيريــا و الفطريات و الفيروسات و الســرطان و الشــلل الرعــاش و كمبيــد للأعشــاب أيضــا. و الاميدازولات لعلاج ضغط الدم المرتفع و الحساســية و داء البــول الســكري و الأمــراض البكتيرية. الترايازولات و الترايازينات كمضادات للبكتيريا و الفطريات و كمبيدات للحشائش و أنشطة مختلفة أخرى ذات قيمة علاجية. و نتيجة لهذه القيمة العلاجية فإنه من الفائدة عند دمج بعض هذه الحلقات في جزئ واحد الحصول على مركبات جديدة ذات قيمة علاجية.

بناء على ذلك فقد تم اصطناع العديد من المشتقات الحلقية الغير متجانسة الجديدة ثلاثية النواة الملتحمة و المحتوية على نواة البيرانوكينولين مثل بيريميدو بيرانو كينولين- بيريدو بيرانــو كينولين- ترايازينو بيرانو كينولين- و رباعية النواة الملتحمة و المحتوية على نواة البيرانــو كينولين مثل إميدازو بيريميدو بيرانو كينولين- ترايازولو ترايازينو بيرانو كينولين- بيرولــو بيرازينو بيرانو كينولين و خماسية النواة الملتحمة و المحتوية على نواة البيرانو كينولين مثل بيرولو ترايازولو بيرازينو بيرانو كينولين.

كما احتوت هذه الرسالة على تقييم لنشاط هذه المركبات ضد بعض أنواع مــن البكتيريــا و الفطريات لمعرفة مدى فعاليتها و قد أوضحت الدراسة أن معظم هذه المركبــات لهــا تــأثير واضح و فعال كما هو واضح من الجداول المذكورة في الرسالة.